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(54) **ARYL OR HETEROARYL DERIVATIVE**

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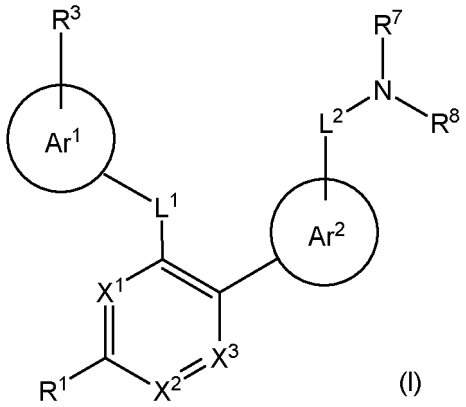
(57) A compound indicated by formula (I) or a pharmacologically acceptable salt thereof is provided as a compound that can be a therapeutic or prophylactic drug for TRPC6-related diseases, such as nephrotic syndrome, membranous nephropathy, acute renal failure, septicemia, chronic renal failure, diabetic nephropathy, pulmonary hypertension, acute lung injury, heart failure, malignant tumor, and muscular dystrophy. (In the formula, Ar^1, Ar^2, X^1-X^3, R^1, R^3, R^7, R^8, L^1, and L^2 are as defined in the specifications.)

(Cont. next page)



(I)

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Description

[Technical field]

[0001] The present invention relates to aryl or heteroaryl derivatives useful as pharmaceutical agents. More specifically, the present invention relates to aryl or heteroaryl derivatives or pharmaceutically acceptable salts thereof useful for the treatment or prevention of diseases in which a TRPC6 inhibitor may be involved, such as nephrotic syndrome, membranous nephropathy, acute renal failure, sepsis, chronic renal failure, diabetic nephropathy, pulmonary hypertension, acute lung injury, heart failure, malignant tumor, or muscular dystrophy.

[Background Art]

[0002] The TRPC6 channel, a member of the Transient receptor potential (TRP) family, which is a non-selective cation-permeable channel, is activated by diacylglycerol and the like produced by activation of phospholipase C and exerts physiological and pathophysiological effects. TRPC6 has effects such as pathological cardiac hypertrophy and fibrosis, progression of myocardial damage in muscular dystrophy, acute pulmonary vasoconstriction, pathological progression associated with chronic hypoxia-induced pulmonary hypertension, allergic immune response, migration of cells such as neutrophils, increased endothelial permeability on inflammation, pathological flattening of podocytes foot processes and following progression of glomerular injury, and proliferation or infiltration of malignant tumors, and is diversely distributed in the brain, heart, lungs, kidneys, placenta, ovaries, spleen, and the like (NPLs 1 to 13). In familial focal segmental glomerulosclerosis (FSGS), a gain-of-function mutant of TRPC6 has been identified, and in idiopathic nephrotic syndrome or idiopathic pulmonary arterial hypertension patients, a variant in the promoter region that increases mRNA expression of TRPC6 has been identified. Thus, it is considered that enhanced activation or increased expression of TRPC6 contributes to pathological progression of nephrotic syndrome, pulmonary hypertension, and the like (NPLs 14 to 22). Furthermore, increased expression of TRPC6 has been reported in minimal change nephrotic syndrome, membranous nephropathy, and diabetic nephropathy (NPLs 23 to 24). Thus, TRPC6 inhibitors, which inhibit ion influx via the TRPC6 channel, are expected to be useful for prevention and/or treatment of such as nephrotic syndrome, membranous nephropathy, acute renal failure, sepsis, chronic renal failure, diabetic nephropathy, pulmonary hypertension, acute lung injury, heart failure, malignant tumor, muscular dystrophy or the like. Compounds inhibiting TRPC6 are described in PLTs 1 to 11.

[Citation List]

[Patent Literature]

[0003]

[PTL 1] WO2011/107474
[PTL 2] WO2012/037349
[PTL 3] WO2012/037351
[PTL 4] WO2014/016766
[PTL 5] Chinese Patent Application Publication No. 104292233
[PTL 6] Chinese Patent Application Publication No. 106317050
[PTL 7] Chinese Patent Application Publication No. 107253952
[PTL 8] WO2019/079578
[PTL 9] WO2019/081637
[PTL 10] WO2019/158572
[PTL 11] WO2019/161010

[Non Patent Literature]

[0004]

[NPL 1] J. Clin. Invest. 116: 3114-3126, 2006
[NPL 2] Dev. Cell. 23: 705-715, 2012
[NPL 3] Circ. Res. 114: 823-832, 2014
[NPL 4] Proc. Natl. Acd. Sci. USA 103: 19093-19098, 2006
[NPL 5] J. Cardiovasc. Pharmacol. 57: 140-147, 2011

[NPL 6] Hypertension 63: 173-80, 2014
[NPL 7] Clin. Exp. Allergy 38: 1548-1558, 2008
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[NPL 22] Circulation 119: 2313-2322, 2009
[NPL 23] J. Am. Soc. Nephrol. 18: 29-36, 2007
[NPL 24] Mol Immunol. Feb;94:75-81, 2018.

[Summary of Invention]

[Technical Problem]

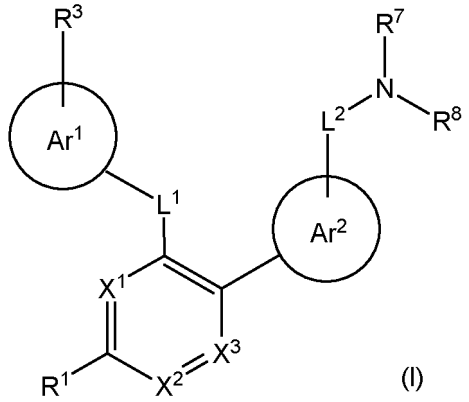
[0005] An object of the present invention is to provide a novel compound having a TRPC6-inhibitory effect or a pharmaceutically acceptable salt thereof, a pharmaceutical composition comprising the compound, and a therapeutic agent or prophylactic agent for diseases associated with TRPC6.

[Solution to Problem]

[0006] As a result of diligent studies for the above-mentioned purpose, the present inventors arrived at the following invention.

[1] A compound represented by the formula (I) or a pharmaceutically acceptable salt thereof.

[Chem. 1]



(I)

[wherein,

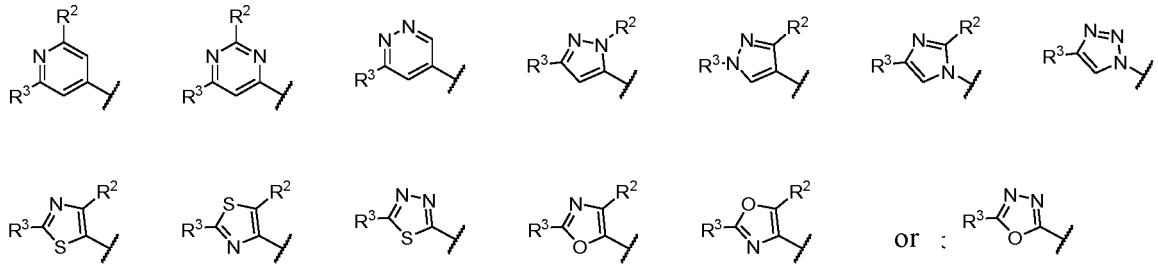
X^1, X^2, and X^3 are independently CH, N, or CY;
At least one of X^1, X^2, and X^3 is CH or CY;
Y is a halogen atom, or a C_{1-3} alkyl group optionally substituted with 1 to 3 halogen atoms;
R^1 is a cyano group, a fluorine atom, or a chlorine atom;

L^1 is -O-, -S-, -SO-, -CH(R^{11})-, -C(= CH_2)-, -CO-, 1,1-cyclopropylidene group, or -NR^{12}-;
R^{11} is a hydrogen atom, a hydroxy group, a C_{1-3} alkyl group optionally substituted with 1 to 3 halogen atoms, or a C_{1-3} alkoxy group optionally substituted with 1 to 2 cyano groups;
R^{12} is a hydrogen atom, or a C_{1-3} alkyl group optionally substituted with 1 to 3 halogen atoms;
Ar^1 is a nitrogen-containing heteroaryl ring optionally substituted with 1 to 3 R^2;
R^2 is independently a halogen atom, a cyano group, or a C_{1-4} alkyl group optionally substituted with 1 to 3 halogen atoms;
R^3 is a hydrogen atom, a halogen atom, an amino group, a cyano group, a carboxy group, a (C_{1-3} alkylcarbonyl)amino group, a (C_{1-6} alkylamino)carbonyl group, a di(C_{1-3} alkyl)aminocarbonyl group, a (C_{1-3} alkoxy)carbonyl group, a (C_{3-8} cycloalkyl)amino group, a (C_{3-8} heterocycloalkyl)amino group, a C_{3-8} cycloalkyl group, a 3- to 8-membered heterocycloalkyloxy group, a C_{3-8} cycloalkyloxy group optionally substituted with 1 to 6 R^{31}, a C_{1-6} alkyl group optionally substituted with 1 to 6 R^{31}, a C_{1-6} alkoxy group optionally substituted with 1 to 6 R^{31}, a di(C_{1-6} alkyl)amino group optionally substituted with 1 to 6 R^{31}, a (C_{1-6} alkyl)amino group optionally substituted with 1 to 6 R^{31}, a 3- to 8-membered heterocycloalkyl group optionally substituted with 1 to 4 R^{32}, an aryl group optionally substituted with 1 to 4 R^{32}, or a heteroaryl group optionally substituted with 1 to 4 R^{32};
R^{31} is independently a halogen atom, a hydroxy group, a cyclopropylidene group, a C_{3-8} cycloalkyl group optionally substituted with 1 to 3 halogen atoms, a 3- to 8-membered heterocycloalkyl group, an oxetanylidene group, a C_{1-4} alkoxy group, or a 3- to 8-membered cycloalkyloxy group;
R^{32} is independently a halogen atom, a hydroxy group, an acetylamino group, a C_{1-3} alkyl group optionally substituted with 1 to 3 halogen atoms, a C_{1-3} alkoxy group optionally substituted with 1 to 3 halogen atoms, an oxo group, a cyano group, a carboxy group, a (C_{1-3} alkoxy)carbonyl group, a (C_{1-3} alkyl)sulfonyl group, a carboxamide group, or a benzyloxy group;
when R^2 and R^3 are bonded to atoms adjacent to each other on Ar^1, R^2 and R^3 may be bonded via a single bond or -O- to form a 5- to 7-membered ring together with the atoms of Ar^1 to which they are bonded;
Ar^2 is an aryl ring optionally substituted with 1 to 4 R^4, or a heteroaryl ring optionally substituted with 1 to 4 R^4;
R^4 is independently a halogen atom, a hydroxy group, a carboxy group, a cyano group, a cyanomethyl group, an amino group, a di(C_{1-3} alkyl)amino group, a C_{1-3} alkyl group optionally substituted with 1 to 3 halogen atoms, or C_{1-3} alkoxy group;
L^2 is a single bond, a C_{1-6} alkylene group optionally substituted with 1 to 3 R^{21}, a C_{3-8} cycloalkylene group optionally substituted with 1 to 3 R^{21}, or a 4- to 8-membered heterocycloalkylene group optionally substituted with 1 to 3 R^{21},
L^2 may be bonded at any position to Ar^2 or -NR^7R^8 which is located at either end of it;
One sp^3 carbon atom at any position of L^2 may be replaced by a structure of -O- or - NR^{22}-;
R^{21} is independently a halogen atom, a hydroxy group, an oxo group, a cyano group, a 1,1-cyclopropylidene group, an oxetanylidene group, a carboxy group, a carboxamide group, a C_{1-6} alkyl group optionally substituted with 1 to 3 halogen atoms, a C_{3-8} cycloalkyl group, a C_{1-6} alkoxy group, a (C_{1-3} alkoxy)C_{1-3} alkyl group, a (C_{1-3} alkoxy)C_{1-3} alkoxy group, a (hydroxy) C_{1-6} alkyl group, a (carboxy)C_{1-3} alkyl group, a (carboxy)C_{1-3} alkoxy group, a (C_{1-3} alkoxy)carbonyl group, a (C_{1-3} alkoxycarbonyl)C_{1-3} alkyl group, a (C_{1-6} alkylamino)carbonyl group, a di(C_{1-3} alkyl) aminocarbonyl group, a phenyl group optionally substituted with 1 to 3 halogen atoms, a heteroaryl group optionally substituted with 1 to 3 halogen atoms, or a phenoxy group optionally substituted with 1 to 3 halogen atoms;
R^{22} is a hydrogen atom or a C_{1-3} alkyl group;
L^2 and R^7 may be bonded via a single bond, -O-, -$S(=O)_n$-, or -NR^{23}- to form a 4- to 8-membered ring containing a nitrogen atom to which L^2 and R^7 are bonded, and the ring is optionally substituted with 1 to 3 halogen atoms or 1 to 2 hydroxy groups;
n represents an integer from 0 to 2;
R^{23} is a hydrogen atom or a C_{1-3} alkyl group;
when L^2 and R^4 are bonded to atoms adjacent to each other on Ar^2, they may be bonded via a single-bond or -O- to form a 5- to 8-membered ring together with the atoms of Ar^2 to which they are bonded;
R^7 is a hydrogen atom, or C_{1-3} alkyl group;
R^7 and an atom of Ar^2 may be bonded via a single bond to form a 5- to 8-membered ring;
R^8 is a hydrogen atom, a C_{1-6} alkyl group, an adamantyl group, a C_{1-6} cycloalkyl group, a cyanomethyl group, an oxetanyl group, a (C_{1-3} alkylamino)carbonylmethyl group, a di(C_{1-3} alkyl)aminocarbonylmethyl group, a (C_{1-3} alkylamino)C_{1-8} alkyl group, a di(C_{1-3} alkyl)aminoC_{1-8} alkyl group, a (hydroxy)C_{1-8} alkyl group, a (carboxy)C_{1-3} alkyl group, a (C_{1-3} alkoxycarbonyl)C_{1-3} alkyl group, or a (C_{1-3} alkoxy)C_{1-3} alkyl group;
R^7 and R^8 may be bonded each other via a single bond, -O-, -$S(=O)_m$-, or -NR^{41}-to form a 3- to 8-membered ring, and further, the ring is optionally substituted with an amino group, an oxo group, or a C_{1-3} alkyl group;
m represents an integer from 0 to 2;

R^{41} is a hydrogen atom or a C_{1-3} alkyl group.]

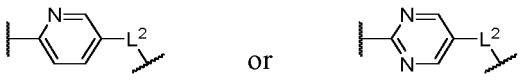
[2] The compound according to [1] or a pharmaceutically acceptable salt thereof, wherein X^1, X^2, and X^3 are CH.
[3] The compound according to [1] or [2] or a pharmaceutically acceptable salt thereof, wherein R^1 is a cyano group.
[4] The compound according to [1] or [2] or a pharmaceutically acceptable salt thereof, wherein R^1 is a fluorine atom.
[5] The compound according to any one of [1] to [4] or a pharmaceutically acceptable salt thereof, wherein the nitrogen-containing heteroaryl ring of Ar^1 is one of the following groups:

[Chem. 2]



[6] The compound according to any one of [1] to [5] or a pharmaceutically acceptable salt thereof, wherein L^1 is -O-.
[7] The compound according to any one of [1] to [5] or a pharmaceutically acceptable salt thereof, wherein L^1 is -CO-.
[8] The compound according to any one of [1] to [5] or a pharmaceutically acceptable salt thereof, wherein L^1 is $-CH_2-$.
[9] The compound according to any one of [1] to [8] or a pharmaceutically acceptable salt thereof, wherein R^2 is a methyl group.
[10] The compound according to any one of [1] to [9] or a pharmaceutically acceptable salt thereof, wherein R^3 is a C_{3-8} cycloalkyl group, a 3- to 8-membered heterocycloalkyloxy group, a C_{3-8} cycloalkyloxy group optionally substituted with 1 to 6 R^{31}, a C_{1-6} alkyl group optionally substituted with 1 to 6 R^{31}, a C_{1-6} alkoxy group optionally substituted with 1 to 6 R^{31}, a di(C_{1-6} alkyl)amino group optionally substituted with 1 to 6 R^{31}, a (C_{1-6} alkyl)amino group optionally substituted with 1 to 6 R^{31}, a 3- to 8-membered heterocycloalkyl group optionally substituted with 1 to 4 R^{32}, an aryl group optionally substituted with 1 to 4 R^{32}, or a heteroaryl group optionally substituted with 1 to 4 R^{32}.
[11] The compound according to any one of [1] to [10] or a pharmaceutically acceptable salt thereof, wherein R^{31} is a halogen atom, a cyclopropylidene group, or a C_{1-4} alkoxy group.
[12] The compound according to any one of [1] to [11] or a pharmaceutically acceptable salt thereof, wherein R^{32} is a halogen atom, a C_{1-3} alkyl group optionally substituted with 1 to 3 halogen atoms, a C_{1-3} alkoxy group optionally substituted with 1 to 3 halogen atoms, an oxo group or a cyano group.
[13] The compound according to any one of [1] to [12] or a pharmaceutically acceptable salt thereof, wherein the heteroaryl ring of Ar^2 is

[Chem. 3]



[14] The compound according to any one of [1] to [13] or a pharmaceutically acceptable salt thereof, wherein L^2 is a C_{1-3} alkylene group optionally substituted with 1 to 2 R^{21}.
[15] The compound according to any one of [1] to [13] or a pharmaceutically acceptable salt thereof, wherein L^2 is $-CH_2-$.
[16] The compound according to any one of [1] to [13] or a pharmaceutically acceptable salt thereof, wherein L^2 is $-CH_2CH_2-$.
[17] The compound according to any one of [1] to [16] or a pharmaceutically acceptable salt thereof, wherein R^7 is a hydrogen atom.
[18] The compound according to any one of [1] to [17] or a pharmaceutically acceptable salt thereof, wherein R^8 is a hydrogen atom.
[19] The compound according to [1] or a pharmaceutically acceptable salt thereof, wherein the compound represented

by the formula (I) is selected from the following (1) to (150):

(1) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
(2) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
(3) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
(4) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-methyl-5-(5-methylpyridin-2-yl)pyrazol-3-yl]oxybenzonitrile
(5) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-[5-(4-fluorophenyl)-2-methylpyrazol-3-yl]oxybenzonitrile
(6) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-[5-(3-fluorophenyl)-2-methylpyrazol-3-yl]oxybenzonitrile
(7) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
(8) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-methyl-5-(2-methylpropyl)pyrazol-3-yl]oxybenzonitrile
(9) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxybenzonitrile
(10) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-5-propylpyrazol-3-yl)oxybenzonitrile
(11) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(5-cyclobutyl-2-methylpyrazol-3-yl)oxybenzonitrile
(12) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3 -(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
(13) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-6-pyrrolidin-1-ylpyridin-4-yl)oxybenzonitrile
(14) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-6-pyridin-2-ylpyridin-4-yl)oxybenzonitrile
(15) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-propylpyrazol-3-yl)oxybenzonitrile
(16) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxybenzonitrile
(17) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-pyrrolidin-1-ylpyridin-4-yl)oxybenzonitrile
(18) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-methyl-5-(trifluoromethyl)pyrazol-3-yl]oxybenzonitrile
(19) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-cyclobutyl-2-methylpyrazol-3-yl)oxybenzonitrile
(20) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
(21) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile
(22) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(6-phenylpyridazin-4-yl)oxybenzonitrile
(23) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
(24) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(5-ethyl-2-methylpyrazol-3-yl)oxybenzonitrile
(25) 4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
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(27) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[6-(2-cyanophenyl)-2-methylpyrimidin-4-yl]oxybenzonitrile
(28) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2,5-dimethylpyrazol-3-yl)oxybenzonitrile
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(31) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-butyl-2-methylpyrazol-3-yl)oxybenzonitrile
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(39) 4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxybenzonitrile
(40) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-propylpyrazol-3-yl)oxybenzonitrile
(41) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxybenzonitrile
(42) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-tert-butyl-2-methylpyrazol-3-yl)oxybenzonitrile
(43) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-pyridin-2-ylpyridin-4-yl)oxybenzonitrile
(44) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-methyl-5-(1,3-thiazol-2-yl)pyrazol-3-yl]oxybenzonitrile
(45) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-(1,3-thiazol-2-yl)pyrazol-3-yl]oxybenzonitrile
(46) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-cyclopentyl-2-methylpyrazol-3-yl)oxybenzonitrile
(47) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
(48) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-(3-fluorophenyl)-2-methylpyrazol-3-yl]oxybenzonitrile
(49) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-[(2S)-2-(difluoromethyl)morpholin-4-yl]-6-methylpyridin-4-yl]oxybenzonitrile
(50) 4-[5-(aminomethyl)pyridin-2-yl]-3-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl]oxybenzonitrile
(51) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-[(2R)-2-(difluoromethyl)morpholin-4-yl]-6-methylpyridin-4-yl]oxybenzonitrile
(52) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)pyridin-4-yl]oxybenzonitrile
(53) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-piperidin-1-ylpyrimidin-4-yl)oxybenzonitrile

(54) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-pyrrolidin-1-ylpyrimidin-4-yl)oxybenzonitrile
(55) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)pyridin-4-yl]oxybenzonitrile
(56) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-[2-methoxyethyl(methyl)amino]-6-methylpyridin-4-yl]oxybenzonitrile
(57) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(propan-2-ylamino)pyridin-4-yl]oxybenzonitrile
(58) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-[(3R)-3-methylmorpholin-4-yl]pyridin-4-yl]oxybenzonitrile
(59) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-[(3S)-3-methylmorpholin-4-yl]pyridin-4-yl]oxybenzonitrile
(60) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-5-piperidin-1-ylpyrazol-3-yl)oxybenzonitrile
(61) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-5-pyrrolidin-1-ylpyrazol-3-yl)oxybenzonitrile
(62) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-[5-(dimethylamino)-2-methylpyrazol-3-yl]oxybenzonitrile
(63) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(1,3-thiazol-2-yl)pyrazol-3-yl]oxybenzonitrile
(64) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-pyridin-2-ylpyrimidin-4-yl)oxybenzonitrile
(65) 4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
(66) 4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-5-piperidin-1-ylpyrazol-3-yl)oxybenzonitrile
(67) 4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-5-pyrrolidin-1-ylpyrazol-3-yl)oxybenzonitrile
(68) 4-[5-(aminomethyl)pyridin-2-yl]-3-[5-(dimethylamino)-2-methylpyrazol-3-yl]oxybenzonitrile
(69) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(4-methylpyridin-2-yl)pyrazol-3-yl]oxybenzonitrile
(70) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-(diethylamino)-2-methylpyrazol-3-yl]oxybenzonitrile
(71) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-(diethylamino)-2-methylpyrazol-3-yl]oxybenzonitrile
(72) 4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-6-pyrrolidin-1-ylpyrimidin-4-yl)oxybenzonitrile
(73) 4-[5-(aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-pyrrolidin-1-ylpyrimidin-4-yl]oxybenzonitrile
(74) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[6-(7-azabicyclo[2.2.1]heptan-7-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile
(75) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(7-azabicyclo[2.2.1]heptan-7-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile
(76) 4-[5-(aminomethyl)pyridin-2-yl]-3-(6-piperidin-1-ylpyridazin-4-yl)oxybenzonitrile
(77) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(5-phenyl-1,3,4-thiadiazol-2-yl)oxy]benzonitrile
(78) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-[5-(diethylamino)-2-methylpyrazol-3-yl]oxybenzonitrile
(79) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-[methyl(2-methylpropyl)amino]pyrazol-3-yl]oxybenzonitrile
(80) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-[cyclopropylmethyl(methyl)amino]-2-methylpyrazol-3-yl]oxybenzonitrile
(81) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-[methyl(propyl)amino]pyrazol-3-yl]oxybenzonitrile
(82) 4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-5-morpholin-4-ylpyrazol-3-yl)oxybenzonitrile
(83) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-[methyl(propan-2-yl)amino]pyrazol-3-yl]oxybenzonitrile
(84) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-[2,2-difluoroethyl(methyl)amino]-2-methylpyrazol-3-yl]oxybenzonitrile
(85) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-[methyl(2,2,2-trifluoroethyl)amino]pyrazol-3-yl]oxybenzonitrile
(86) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-6-[(2S)-2-methylpyrrolidin-1-yl]pyrimidin-4-yl]oxybenzonitrile
(87) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[3-methyl-1-(2-methylpropyl)pyrazol-4-yl]oxybenzonitrile
(88) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[3-methyl-1-(2-methylpropyl)pyrazol-4-yl]oxybenzonitrile
(89) 4-[5-(aminomethyl)pyridin-2-yl]-3-[2-methyl-5-(trifluoromethyl)pyrazol-3-yl]oxybenzonitrile
(90) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(trifluoromethyl)pyrazol-3-yl]oxybenzonitrile
(91) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-(trifluoromethyl)pyrazol-3-yl]oxybenzonitrile
(92) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-(7-azabicyclo[2.2.1]heptan-7-yl)-6-methylpyridin-4-yl]oxybenzonitrile
(93) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-(7-azabicyclo[2.2.1]heptan-7-yl)-6-methylpyridin-4-yl]oxybenzonitrile
(94) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(3-methyl-1-pyridin-2-ylpyrazol-4-yl)oxybenzonitrile
(95) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-(3-methyl-1-pyridin-2-ylpyrazol-4-yl)oxybenzonitrile
(96) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[3-methyl-1-(2,2,2-trifluoroethyl)pyrazol-4-yl]oxybenzonitrile
(97) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-[ethyl(propan-2-yl)amino]-2-methylpyrazol-3-yl]oxybenzonitrile
(98) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(2-methylpropoxy)pyrimidin-4-yl]oxybenzonitrile
(99) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[6-(diethylamino)-2-methylpyrimidin-4-yl]oxybenzonitrile
(100) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-[methyl(propan-2-yl)amino]pyrimidin-4-yl]oxybenzonitrile

(101) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-[(2R)-2-methylpyrrolidin-1-yl]pyrimidin-4-yl]oxybenzonitrile
(102) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-[(2S)-2-methylpyrrolidin-1-yl]pyrimidin-4-yl]oxybenzonitrile
(103) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(3,3,4,5-tetrafluoropyrrolidin-1-yl)pyrazol-3-yl]oxybenzonitrile
(104) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-[2,2-difluoroethyl(ethyl)amino]-2-methylpyrazol-3-yl]oxybenzonitrile
(105) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-[2,2-difluoroethyl(ethyl)amino]-2-methylpyrazol-3-yl]oxybenzonitrile
(106) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-(3,3,4,4-tetrafluoropyrrolidin-1-yl)pyrazol-3-yl]oxybenzonitrile
(107) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[1-(2-methylpropyl)pyrazol-4-yl]oxybenzonitrile
(108) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(1-pyridin-2-ylpyrazol-4-yl)oxybenzonitrile
(109) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[1-(2,2-dimethylpropyl)-3-methylpyrazol-4-yl]oxybenzonitrile
(110) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(1,3-thiazol-4-yl)pyrazol-3-yl]oxybenzonitrile
(111) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[3-ethyl-1-(2-methylpropyl)pyrazol-4-yl]oxybenzonitrile
(112) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[1-(2-methylpropyl)-3-(trifluoromethyl)pyrazol-4-yl]oxybenzonitrile
(113) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(4-methyl-1,3-thiazol-5-yl)pyrazol-3-yl]oxybenzonitrile
(114) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(5-methyl-1,3-thiazol-4-yl)pyrazol-3-yl]oxybenzonitrile
(115) 2-[2-[4-fluoro-2-[3-methyl-1-(2-methylpropyl)pyrazol-4-yl]oxyphenyl]pyrimidin-5-yl]ethanamine
(116) 5-[2-[5-(2-aminoethyl)pyrimidin-2-yl]-5-fluorophenoxy]-N,N-diethyl-1-methylpyrazole-3-amine
(117) 2-[6-[4-fluoro-2-(2-methyl-5-morpholin-4-ylpyrazol-3-yl)oxyphenyl]pyridin-3-yl]ethanamine
(118) 2-[2-[4-fluoro-2-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxyphenyl]pyrimidin-5-yl]ethanamine
(119) 2-[2-[4-fluoro-2-(2-methyl-5-pyrrolidin-1-ylpyrazol-3-yl)oxyphenyl]pyrimidin-5-yl]ethanamine
(120) 2-[6-[4-fluoro-2-(2-methyl-5-pyrrolidin-1-ylpyrazol-3-yl)oxyphenyl]pyridin-3-yl]ethanamine
(121) 5-[2-[5-(2-aminoethyl)pyrimidin-2-yl]-5-fluorophenoxy]-N-(2,2-difluoroethyl)-N,1-dimethylpyrazole-3-amine
(122) 5-[2-[5-(2-aminoethyl)pyridin-2-yl]-5-fluorophenoxy]-N-(2,2-difluoroethyl)-N,1-dimethylpyrazole-3 -amine
(123) 5-[2-[5-(2-aminoethyl)pyrimidin-2-yl]-5-fluorophenoxy]-N-(2,2-difluoroethyl)-N-ethyl-1-methylpyrazole-3-amine
(124) 5-[2-[5-(2-aminoethyl)pyridin-2-yl]-5-fluorophenoxy]-N-(2,2-difluoroethyl)-N-ethyl-1-methylpyrazole-3-amine
(125) 5-[2-[5-(2-aminoethyl)pyridin-2-yl]-5-fluorophenoxy]-N,N-diethyl-1-methylpyrazole-3 -amine
(126) 5-[2-[5-(2-aminoethyl)pyridin-2-yl]-5-fluorophenoxy]-N,N,1-trimethylpyrazole-3-amine
(127) 2-[6-[4-fluoro-2-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl]oxyphenyl]pyridin-3-yl]ethanamine
(128) [2-[4-fluoro-2-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxyphenyl]pyrimidin-5-yl]methanamine
(129) 2-[2-[4-fluoro-2-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxyphenyl]pyrimidin-5-yl]ethanamine
(130) 2-[6-[4-fluoro-2-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxyphenyl]pyridin-3-yl]ethanamine
(131) 2-[6-[2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxy-4-fluorophenyl]pyridin-3-yl]ethanamine
(132) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-ethyl-2-methylpyrazole-3-carbonyl)benzonitrile
(133) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-(5-ethyl-2-methylpyrazole-3-carbonyl)benzonitrile
(134) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-morpholin-4-ylpyrazole-3-carbonyl)benzonitrile
(135) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-morpholin-4-ylpyrazole-3-carbonyl)benzonitrile
(136) 4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-5-morpholin-4-ylpyrazole-3-carbonyl)benzonitrile
(137) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-(5-tert-butyl-2-methylpyrazole-3-carbonyl)benzonitrile
(138) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-tert-butyl-2-methylpyrazole-3-carbonyl)benzonitrile
(139) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-(diethylamino)-2-methylpyrazole-3-carbonyl]benzonitrile
(140) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(1-pyridin-2-ylpyrazole-4-carbonyl)benzonitrile
(141) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridine-4-carbonyl)benzonitrile
(142) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-(dimethylamino)-2-methylpyrazole-3-carbonyl]benzonitrile
(143) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-(dimethylamino)-2-methylpyrazole-3-carbonyl]benzonitrile
(144) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-(diethylamino)-2-methylpyrazole-3-carbonyl]benzonitrile
(145) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-piperidin-1-ylpyrazole-3-carbonyl)benzonitrile
(146) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-piperidin-1-ylpyrazole-3-carbonyl)benzonitrile
(147) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-pyrrolidin-1-ylpyrazole-3-carbonyl)benzonitrile
(148) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-pyrrolidin-1-ylpyrazole-3-carbonyl)benzonitrile
(149) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-[2,2-difluoroethyl(ethyl)amino]-2-methylpyrazole-3-carbonyl]ben-

zonitrile
(150) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-[2,2-difluoroethyl(ethyl)amino]-2-methylpyrazole-3-carbonyl]benzonitrile.

[20] A pharmaceutical composition comprising the compound according to any one of [1] to [19] or a pharmaceutically acceptable salt thereof.
[21] A pharmaceutical composition having TRPC6 channel inhibitory activity, comprising the compound according to any one of [1] to [19] or a pharmaceutically acceptable salt thereof.
[22] A therapeutic or prophylactic agent for nephrotic syndrome, membranous nephropathy, acute renal failure, sepsis, chronic renal failure, diabetic nephropathy, pulmonary hypertension, acute lung injury, heart failure, malignant tumors, or muscular dystrophy, comprising the compound according to any one of [1] to [19] or a pharmaceutically acceptable salt thereof.

[Advantageous Effects of Invention]

[0007] The present invention provides a novel compound or a pharmaceutically acceptable salt thereof, having TRPC6 inhibitory activity, and a pharmaceutical composition and a therapeutic or prophylactic drug for the disease associated with TRPC6, including thereof.

[Description of Embodiments]

[0008] Terms used alone or in combination in the present description will be explained below. Unless otherwise stated, the explanation of each substituent shall be common to each site. In addition, combinations of substituents and variables are permissible only if such combinations result in chemically stable compounds. When the substituent itself is substituted with two or more groups, these many groups can exist on the same or different carbon atom as long as a stable structure is formed.
[0009] In the present invention, the number situated to the right of carbon atom indicates the number of carbon atoms. For example, "C_{1-6}" represents having "1 to 6 carbon atoms." For example, a "C_{1-4} alkyl group" means an alkyl group having 1 to 4 carbon atoms. The number of carbon atoms in other groups is handled in the same manner. Incidentally, for example, in an expression such as "(C_{1-3} alkyl)carbonyl group", the number of carbon atoms of C_{1-3} represents the number of carbon atoms of the C_{1-3} alkyl in the parentheses, and the carbon in the carbonyl is not considered. The number of carbon atoms in a similar representation is calculated in the same manner. Unless otherwise specified, the method of naming a substituent shall be performed by naming from the terminal portion of the functional group and then naming the functional group adjacent to the binding point.
[0010] In the present invention, the "halogen atom" means a fluorine atom, a chlorine atom, a bromine atom, and an iodine atom.
[0011] In the present invention, "alkyl group" means a saturated linear or branched aliphatic hydrocarbon group and includes, for example, a methyl group, a ethyl group, an n-propyl group, an n-butyl group, an n-pentyl group, an n-hexyl group, an isopropyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, an isopentyl group, a 2-methylbutyl group, a 3-methylbutyl group, a 1-ethylpropyl group, a 1,1-dimethylpropyl group, a 1,2-dimethylpropyl group, a neopentyl group, a 4-methylpentyl group, a 3-methylpentyl group, a 2-methylpentyl group, a 1-methylpentyl group, a 3,3-dimethylbutyl group, a 2,2-dimethylbutyl group, a 1,1-dimethylbutyl group, a 1,2-dimethylbutyl group, a 1,3-dimethylbutyl group, a 2,3-dimethylbutyl group, a 1-ethylbutyl group, a 2-ethylbutyl group and the like.
[0012] In the present invention, the "cycloalkyl group" means a saturated or partially unsaturated monocyclic or polycyclic hydrocarbon group, and includes, for example, a cyclopropyl group, a cyclobutyl group, a cyclopentyl group, a cyclohexyl group, a cycloheptyl group, a cyclooctyl group and the like.
[0013] In the present invention, a "heterocycloalkyl group" means a saturated or partially unsaturated monocyclic or polycyclic hydrocarbon ring in which one or more carbon atoms are substituted with a hetero atom selected from O, S and N, and includes, for example, an aziridino group, an azetidino group, an oxetanyl group, a morpholino group, a thiomorpholino group, a pyrrolidinyl group, a piperidinyl group, a piperazinyl group, an imidazolidinyl group, a pyrazoridinyl group, a tetrahydrofuranyl group, a tetrahydropyranyl group and the like.
[0014] In the present invention, the "alkoxy group", "cycloalkyloxy group" and "heterocycloalkyloxy group" mean an oxy group substituted with an alkyl group, a cycloalkyl group or a heterocycloalkyl group.
[0015] In the present invention, "(alkoxy)alkoxy group" and "(carboxy)alkoxy group" mean an alkoxy group substituted with an alkoxy group or a carboxy group. For example, "(C_{1-3} alkoxy)C_{1-3} alkoxy group" means an alkoxy group having 1 to 3 carbon atoms substituted with an alkoxy group having 1 to 3 carbon atoms.
[0016] In the present invention, "(alkoxy)carbonyl group" means a carbonyl group substituted with an alkoxy group. For example, "(C_{1-3} alkoxy)carbonyl group" means a carbonyl group substituted with an alkoxy group having 1 to 3

carbon atoms.

[0017] In the present invention, "(alkyl) amino group", "(cycloalkyl) amino group" and "(heterocycloalkyl) amino group" mean an amino group substituted with one alkyl group, cycloalkyl group and heterocycloalkyl group, respectively. For example, "(C_{3-8} heterocycloalkyl)amino group" means an amino group substituted with a 3- to 8-membered heterocycloalkyl group.

[0018] In the present invention, "di(alkyl)amino group" means an amino group substituted with two of the same or different alkyl groups. For example, "di(C_{1-6} alkyl)amino group" means an amino group substituted with two of the same or different alkyl groups having 1 to 6 carbon atoms.

[0019] In the present invention, "(alkylcarbonyl)amino group" means an amino group substituted with one alkylcarbonyl group. For example, "(C_{1-3} alkyl)carbonylamino group" means an amino group substituted with one (C_{1-3} alkyl)carbonyl group.

[0020] In the present invention, "(alkylamino)carbonyl group" means a carbonyl group substituted with an alkylamino group. Similarly, "di(alkyl)aminocarbonyl group" means a carbonyl group substituted with a di(alkyl)amino group.

[0021] In the present invention, "alkoxyalkyl group", "alkoxycarbonylalkyl group", "di(alkyl)aminoalkyl group", "hydroxyalkyl group" and "carboxyalkyl group" mean an alkyl group substituted with an alkoxy group, an alkoxycarbonyl group, a di(alkyl)amino group, a hydroxy group and a carboxy group, respectively. Further, "di(alkyl) aminocarbonylmethyl group" means a methyl group substituted with a di(alkyl)aminocarbonyl group.

[0022] In the present invention, "alkylene group" means a divalent group derived by removing one hydrogen atom at an arbitrary position from the "alkyl group", and includes, for example, a methylene group, an ethylene group, an n-propylene group, an isopropylene group, an n-butylene group, an isobutylene group, an n-pentylene group, an n-hexylene group and the like.

[0023] In the present invention, "cycloalkylene group" means a divalent group derived by removing one hydrogen atom at an arbitrary position from the "cycloalkyl group", and includes, for example, a cyclopropylene group, a cyclobutylene group, a cyclohexylene group and the like.

[0024] In the present invention, "heterocycloalkylene group" means a divalent group derived by removing one hydrogen atom at an arbitrary position from the "heterocycloalkyl group".

[0025] In the present invention, "optionally substituted C_{1-3} alkyl group" represents an alkyl group having 1 to 3 carbon atoms which may have one or more substituents at substitutable positions. When a plurality of substituents is present, each substituent may be the same or different. Similar expressions have the same meaning.

[0026] In the present invention, "aryl group" means a monocyclic or bicyclic aromatic hydrocarbon group having 6 to 10 carbon atoms, and includes, for example, a phenyl group, a naphthyl group, an indenyl group, an azulenyl group and the like. "Aryl ring" refers to the ring portion of an aryl group.

[0027] In the present invention, "heteroaryl group" means a 5- to 10-membered monocyclic or bicyclic aromatic heterocyclic group having 1 to 5 heteroatoms selected from O, S, and N. Heteroaryl group includes a pyridyl group, a pyrazil group, a pyrimidyl group, a pyridadyl group, a furyl group, a thienyl group, an isooxazolyl group, an isothiazolyl group, a benzofuranyl group, a benzothienyl group, a benzothiazolyl group, a benzoimidazolyl group, a benzoxazolyl group, a pyranyl group, a pyrazolyl group, an imidazolyl group, an oxazolyl group, a thiazolyl group, a triazinyl group, a triazolyl group, a benzoxazolyl group, a benzoisoxazolyl group and the like. "Heteroaryl ring" refers to the ring portion of a heteroaryl group. "Nitrogen-containing heteroaryl ring" means a heteroaryl ring containing one or more Ns on the ring.

[0028] In the formula (I), X^1, X^2, and X^3 are independently CH, N, or CY, and at least one of X^1, X^2, and X^3 is CH or CY. Preferably, X^1, X^2, and X^3 are CH.

[0029] Y is a halogen atom or a methyl group.

[0030] In the formula (I), R^1 is a cyano group, a fluorine atom, or a chlorine atom, and preferably a cyano group or a fluorine atom.

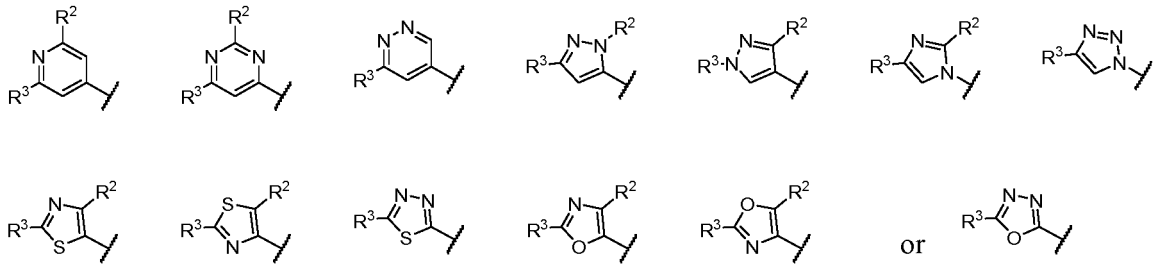
[0031] In the formula (I), linker L^1 is -O-, -S-, -SO-, -CH(R^{11})-, -C(=CH_2)-, -CO-, a 1,1-cyclopropylidene group, or -NR^{12}-, preferably, -O-, -S-, -CH(R^{11})-, -CO-, or -NR^{12}-, and more preferably -O-, -CO-, or -CH_2-.

[0032] R^{11} is a hydrogen atom, a hydroxy group, a C_{1-3} alkyl group optionally substituted with 1 to 3 halogen atoms, or a C_{1-3} alkoxy group optionally substituted with 1 to 2 cyano groups.

[0033] R^{12} is a hydrogen atom or a C_{1-3} alkyl group optionally substituted with 1 to 3 halogen atoms.

[0034] In the formula (I), Ar^1 is a nitrogen-containing heteroaryl ring optionally substituted with 1 to 3 R^2, and preferably has the following structures.

[Chem. 4]



[0035] R^2 is independently a halogen atom, a cyano group, or a C_{1-4} alkyl group optionally substituted with 1 to 3 halogen atoms, preferably a C_{1-4} alkyl group optionally substituted with 1 to 3 halogen atoms, and more preferably a methyl group. When R^2 and R^3 are bonded to atoms adjacent to each other on Ar^1, R^2 and R^3 may be bonded via a single bond or -O- to form a 5- to 7-membered ring together with the atoms on Ar^1 to which they are bonded.

[0036] In the formula (I), R^3 is a hydrogen atom, a halogen atom, an amino group, a cyano group, a carboxy group, a (C_{1-3} alkylcarbonyl)amino group, a (C_{1-6} alkylamino)carbonyl group, a di(C_{1-3} alkyl)aminocarbonyl group, a (C_{1-3} alkoxy)carbonyl group, a (C_{3-8} cycloalkyl)amino group, a (C_{3-8} heterocycloalkyl)amino group, a C_{3-8} cycloalkyl group, a 3- to 8-membered heterocycloalkyloxy group, a C_{3-8} cycloalkyloxy group optionally substituted with 1 to 6 R^{31}, a C_{1-6} alkyl group optionally substituted with 1 to 6 R^{31}, a C_{1-6} alkoxy group optionally substituted with 1 to 6 R^{31}, a di(C_{1-6} alkyl)amino group optionally substituted with 1 to 6 R^{31}, a (C_{1-6} alkyl)amino group optionally substituted with 1 to 6 R^{31}, a 3- to 8-membered heterocycloalkyl group optionally substituted with 1 to 4 R^{32}, an aryl group optionally substituted with 1 to 4 R^{32}, or a heteroaryl group optionally substituted with 1 to 4 R^{32}.

[0037] R^{31} is independently a halogen atom, a hydroxy group, a cyclopropylidene group, a C_{3-8} cycloalkyl group optionally substituted with 1 to 3 halogen atoms, a 3- to 8-membered heterocycloalkyl group, an oxetanylidene group, a C_{1-4} alkoxy group, or a 3- to 8-membered cycloalkyloxy group.

[0038] R^{32} is independently a halogen atom, a hydroxy group, an acetylamino group, a C_{1-3} alkyl group optionally substituted with 1 to 3 halogen atoms, a C_{1-3} alkoxy group optionally substituted with 1 to 3 halogen atoms, an oxo group, a cyano group, a carboxy group, a (C_{1-3} alkoxy)carbonyl group, a (C_{1-3} alkyl)sulfonyl group, a carboxamide group, or a benzyloxy group.

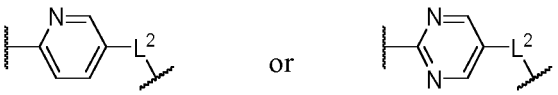
[0039] In the formula (I), preferred R^3 is a C_{3-8} cycloalkyl group, a 3- to 8-membered heterocycloalkyloxy group, a C_{3-8} cycloalkyloxy group optionally substituted with 1 to 6 R^{31}, a C_{1-6} alkyl group optionally substituted with 1 to 6 R^{31}, a C_{1-6} alkoxy group optionally substituted with 1 to 6 R^{31}, a di(C_{1-6} alkyl)amino group optionally substituted with 1 to 6 R^{31}, a (C_{1-6} alkyl)amino group optionally substituted with 1 to 6 R^{31}, a 3- to 8-membered heterocycloalkyl group optionally substituted with 1 to 4 R^{32}, an aryl group optionally substituted with 1 to 4 R^{32} or a heteroaryl group optionally substituted with 1 to 4 R^{32}.

[0040] Preferred R^{31} is a halogen atom, a cyclopropylidene group, or a C_{1-4} alkoxy group.

[0041] Preferred R^{32} is a halogen atom, a C_{1-3} alkyl group optionally substituted with 1 to 3 halogen atoms, a C_{1-3} alkoxy group optionally substituted with 1 to 3 halogen atoms, an oxo group, or a cyano group.

[0042] In the formula (I), Ar^2 is an aryl ring optionally substituted with 1 to 4 R^4, or a heteroaryl ring optionally substituted with 1 to 4 R^4, preferably a heteroaryl ring optionally substituted with 1 to 4 R^4, and more preferably a pyridine ring or a pyrimidine ring having a substitution pattern of the following structure.

[Chem. 5]



[0043] R^4 is independently a halogen atom, a hydroxy group, a carboxy group, a cyano group, a cyanomethyl group, an amino group, a di(C_{1-3} alkyl)amino group, a C_{1-3} alkyl group optionally substituted with 1 to 3 halogen atoms, or a C_{1-3} alkoxy group.

[0044] In the formula (I), L^2 is a single bond, a C_{1-6} alkylene group optionally substituted with 1 to 3 R^{21}, a C_{3-8} cycloalkylene group optionally substituted with 1 to 3 R^{21}, or a 4- to 8-membered heterocycloalkylene group optionally substituted with 1 to 3 R^{21}. L^2 may be bonded at any position to Ar^2 or $-NR^7R^8$ which is located at either end of it. One sp^3 carbon atom at any position of L^2 may be replaced by a structure of -O- or $-NR^{22}$-. Preferred L^2 is a C_{1-3} alkylene

group optionally substituted with 1 to 2 R^{21}, and more preferably $-CH_2-$ or $-CH_2CH_2-$.

[0045] R^{21} is independently a halogen atom, a hydroxy group, an oxo group, a cyano group, a 1,1-cyclopropylidene group, an oxetanylidene group, a carboxy group, a carboxamide group, a C_{1-6} alkyl group optionally substituted with 1 to 3 halogen atoms, a C_{3-8} cycloalkyl group, a C_{1-6} alkoxy group, a $(C_{1-3}$ alkoxy)C_{1-3} alkyl group, a $(C_{1-3}$ alkoxy)C_{1-3} alkoxy group, a (hydroxy) C_{1-6} alkyl group, a (carboxy)C_{1-3} alkyl group, a (carboxy)C_{1-3} alkoxy group, a $(C_{1-3}$ alkoxy)carbonyl group, a $(C_{1-3}$ alkoxycarbonyl)C_{1-3} alkyl group, a $(C_{1-6}$ alkylamino)carbonyl group, a di$(C_{1-3}$ alkyl) aminocarbonyl group, a phenyl group optionally substituted with 1 to 3 halogen atoms, a heteroaryl group optionally substituted with 1 to 3 halogen atoms, or a phenoxy group optionally substituted with 1 to 3 halogen atoms. Preferred R^{21} is a halogen atom, a hydroxy group, an oxo group, an oxetanylidene group, or a C_{1-6} alkyl group optionally substituted with 1 to 3 halogen atoms, and more preferred is a halogen atom or a hydroxy group.

[0046] R^{22} is a hydrogen atom or a C_{1-3} alkyl group.

[0047] L^2 and R^7 may be bonded via a single bond, -O-, $-S(=O)_n-$, or $-NR^{23}-$ to form a 4- to 8-membered ring containing a nitrogen atom to which L^2 and R^7 are bonded, and the ring is optionally substituted with 1 to 3 halogen atoms or 1 to 2 hydroxy groups, wherein n represents an integer from 0 to 2.

[0048] R^{23} is a hydrogen atom or a C_{1-3} alkyl group.

[0049] When L^2 and R^4 are bonded to atoms adjacent to each other on Ar^2, they may be bonded via a single-bond or -O- to form a 5- to 8-membered ring together with the atoms of Ar^2 to which they are bonded.

[0050] In the formula (I), R^7 is a hydrogen atom or a C_{1-3} alkyl group, and more preferably a hydrogen atom. R^7 and an atom of Ar^2 may be bonded via a single bond to form a 5- to 8-membered ring.

[0051] In the formula (I), R^8 is a hydrogen atom, a C_{1-6} alkyl group, an adamantyl group, a C_{1-6} cycloalkyl group, a cyanomethyl group, an oxetanyl group, a $(C_{1-3}$ alkylamino)carbonylmethyl group, a di$(C_{1-3}$ alkyl)aminocarbonylmethyl group, a $(C_{1-3}$ alkylamino)C_{1-8} alkyl group, a di$(C_{1-3}$ alkyl)aminoC_{1-8} alkyl group, a (hydroxy)C_{1-8} alkyl group, a (carboxy)C_{1-3} alkyl group, a $(C_{1-3}$ alkoxycarbonyl)C_{1-3} alkyl group, or a $(C_{1-3}$ alkoxy)C_{1-3} alkyl group. More preferred R^8 is a hydrogen atom.

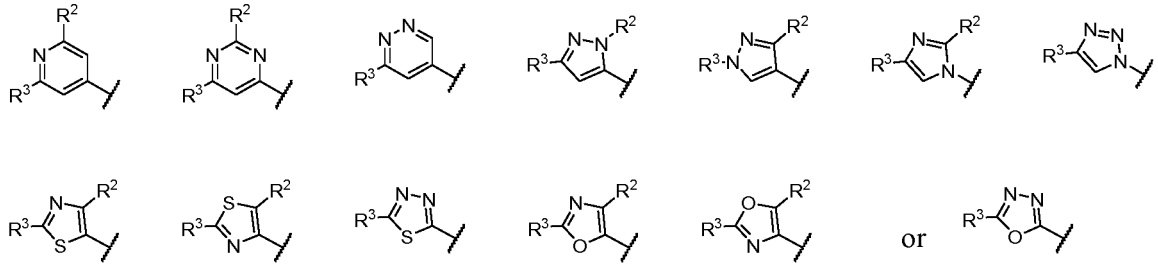
[0052] R^7 and R^8 may be bonded each other via a single bond, -O-, $-S(=O)_m-$, or $-NR^{41}-$ to form a 3- to 8-membered ring, and further, the ring is optionally substituted with an amino group, an oxo group, or a C_{1-3} alkyl group, wherein m represents an integer from 0 to 2.

[0053] R^{41} is a hydrogen atom or a C_{1-3} alkyl group.

[0054] Among the compounds of the present invention, preferable is the following compound group, that is, the compound group in the formula (I),
wherein,

X^1, X^2, and X^3 are CH,
R^1 is a cyano group or a fluorine atom,
linker L^1 is -O-, -CO-, or $-CH_2-$,
Ar^1 has the following structure,

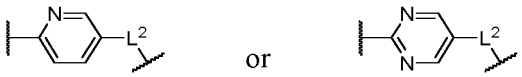
[Chem. 6]



R^2 is a methyl group,
R^3 is a C_{3-8} cycloalkyl group, a 3- to 8-membered heterocycloalkyloxy group, a C_{3-8} cycloalkyloxy group optionally substituted with 1 to 6 R^{31}, a C_{1-6} alkyl group optionally substituted with 1 to 6 R^{31}, a C_{1-6} alkoxy group optionally substituted with 1 to 6 R^{31}, a di$(C_{1-6}$ alkyl)amino group optionally substituted with 1 to 6 R^{31}, a $(C_{1-6}$ alkyl)amino group optionally substituted with 1 to 6 R^{31}, a 3- to 8-membered heterocycloalkyl group optionally substituted with 1 to 4 R^{32}, an aryl group optionally substituted with 1 to 4 R^{32} or a heteroaryl group optionally substituted with 1 to 4 R^{32}.
R^{31} is a halogen atom, a cyclopropylidene group, or a C_{1-4} alkoxy group, and
R^{32} is a halogen atom, a C_{1-3} alkyl group optionally substituted with 1 to 3 halogen atoms, a C_{1-3} alkoxy group optionally substituted with 1 to 3 halogen atoms, an oxo group, or a cyano group.

Ar^2 is a pyridine ring or a pyrimidine ring having a substitution pattern of the following structure.

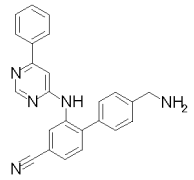
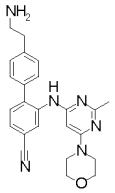
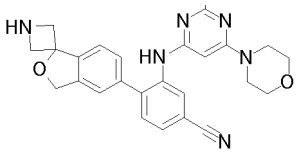
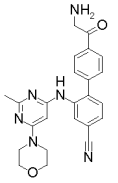
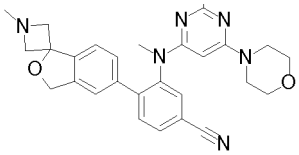
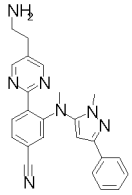
[Chem. 7]



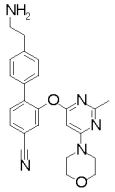
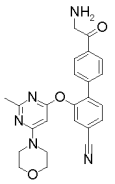
L^2 is $-CH_2-$ or $-CH_2CH_2-$,
R^7 is a hydrogen atom, and
R^8 is a hydrogen atom.

[0055] Specific examples of the compound of the formula (I) include the compounds shown in the following Table 1.

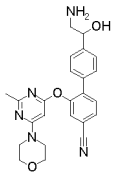
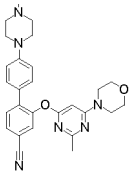
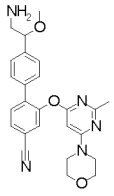
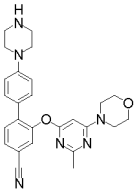
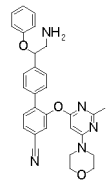
[Table 1-1]

Compound number	Structural formula	Compound name
1		4-[4-(aminomethyl)phenyl]-3-[(6-phenylpyrimidin-4-yl)amino] benzonitrile
2		4-[4-(2-aminoethyl)phenyl]-3-[(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)amino]benzonitrile
3		3-[(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)amino]-4-spiro [3H-2-benzofuran-1,3'-azetidin]-5-ylbenzonitrile
4		4-[4-(2-aminoacetyl)phenyl]-3-[(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)amino]benzonitrile
5		3-[methyl-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)amino]-4-(1'-methylspiro[3H-2-benzofuran-1,3'-azetidin]-5-yl) benzonitrile
6		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[methyl -(2-methyl -5 -phenylpyrazol - 3 -yl)amino]benzonitrile

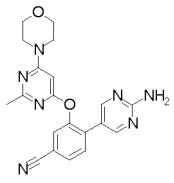
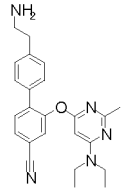
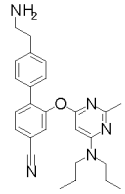
(continued)

Compound number	Structural formula	Compound name
7		4-[4-(2-aminoethyl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
8		4-[4-(2-aminoacetyl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile

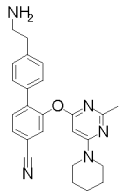
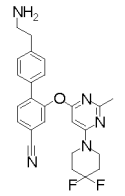
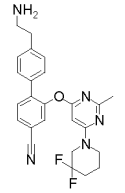
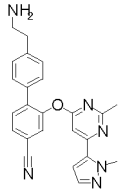
[Table 1-2]

Compound number	Structural formula	Compound name
9		4-[4-(2-amino-1-hydroxyethyl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
10		3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxy-4-[4-(4-methylpiperazin-1 - yl)phenyl]benzonitrile
11		4-[4-(2-amino-1-methoxyethyl)phenyl] -3 -(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
12		3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxy-4-(4-piperazin-1-ylphenyl)benzonitrile
13		4-[4-(2-amino-1-phenoxyethyl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile

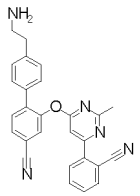
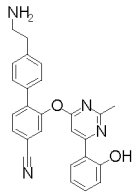
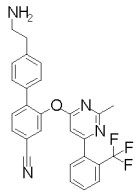
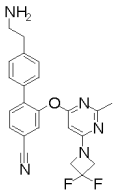
(continued)

Compound number	Structural formula	Compound name
14		4-(2-aminopyrimidin-5-yl)-3 -(2-methyl-6-morpholin-4-ylpyrimidin-4-yl) oxybenzonitrile
15		4-[4-(2-aminoethyl)phenyl]-3-[6-(diethylamino)-2-methylpyrimidin-4-yl] oxybenzonitrile
16		4-[4-(2-aminoethyl)phenyl]-3-[6-(dipropylamino)-2-methylpyrimidin-4-yl]oxybenzonitrile

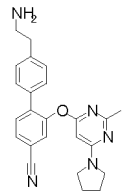
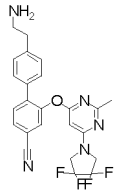
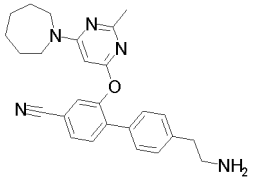
[Table 1-3]

Compound number	Structural formula	Compound name
17		4-[4-(2-aminoethyl)phenyl]-3-(2-methyl-6-piperidin-1-ylpyrimidin-4-yl) oxybenzonitrile
18		4-[4-(2-aminoethyl)phenyl]-3-[6-(4,4-difluoropiperidin-1-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile
19		4-[4-(2-aminoethyl)phenyl]-3-[6-(3,3-difluoropiperidin-1 -yl)-2-methylpyrimidin-4-yl]oxybenzonitrile
20		4-[4-(2-aminoethyl)phenyl]-3-[2-methyl-6-(2-methylpyrazol-3 - yl) pyrimidin-4-yl]oxybenzonitrile

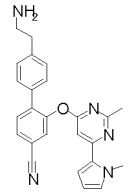
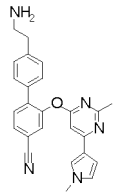
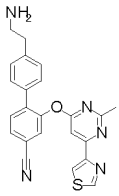
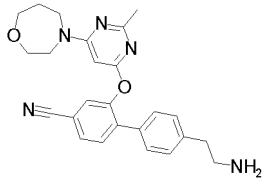
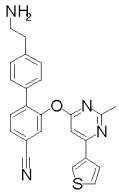
(continued)

Compound number	Structural formula	Compound name
21		4-[4-(2-aminoethyl)phenyl]-3-[6-(2-cyanophenyl)-2-methylpyrimidin-4-yl]oxybenzonitrile
22		4-[4-(2-aminoethyl)phenyl]-3-[6-(2-hydroxyphenyl)-2-methylpyrimidin-4-yl]oxybenzonitrile
23		4-[4-(2-aminoethyl)phenyl]-3-[2-methyl-6-[2-(trifluoromethyl)phenyl] pyrimidin-4-yl]oxybenzonitrile
24		4-[4-(2-aminoethyl)phenyl]-3-[6-(3,3-difluoroazetidin-1-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile

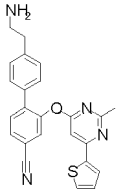
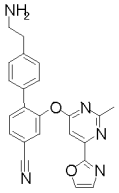
[Table 1-4]

Compound number	Structural formula	Compound name
25		4-[4-(2-aminoethyl)phenyl]-3-(2-methyl-6-pyrrolidin-1 -ylpyrimidin-4-yl)oxybenzonitrile
26		4-[4-(2-aminoethyl)phenyl]-3-[2-methyl-6-(3,3,4,4-tetrafluoropyrrolidin-1-yl)pyrimidin-4-yl]oxybenzonitrile
27		4-[4-(2-aminoethyl)phenyl]-3-[6-(azepan-1-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile

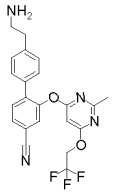
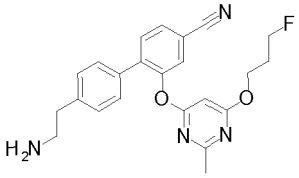
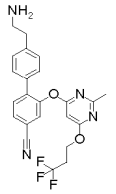
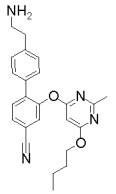
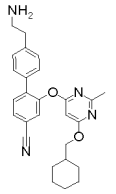
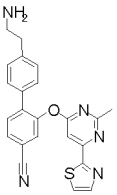
(continued)

Compound number	Structural formula	Compound name
28		4-[4-(2-aminoethyl)phenyl]-3-[2-methyl-6-(1-methylpyrrol-2-yl)pyrimidin-4-yl]oxybenzonitrile
29		4-[4-(2-aminoethyl)phenyl]-3-[2-methyl-6-(1-methylpyrrol-3-yl)pyrimidin-4-yl]oxybenzonitrile
30		4-[4-(2-aminoethyl)phenyl]-3-[2-methyl-6-(1,3-thiazol-4-yl) pyrimidin-4-yl]oxybenzonitrile
31		4-[4-(2-aminoethyl)phenyl]-3-[2-methyl-6-(1,4-oxazepan-4-yl) pyrimidin-4-yl]oxybenzonitrile
32		4-[4-(2-aminoethyl)phenyl]-3-(2-methyl-6-thiophen-3 -ylpyrimidin-4-yl)oxybenzonitrile

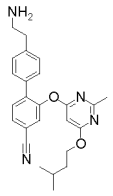
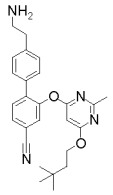
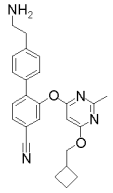
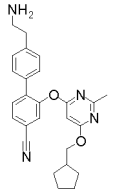
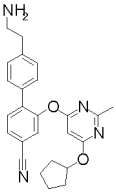
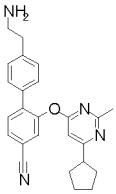
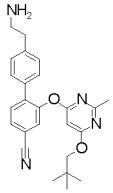
[Table 1-5]

Compound number	Structural formula	Compound name
33		4-[4-(2-aminoethyl)phenyl]-3-(2-methyl-6-thiophen-2-ylpyrimidin-4-yl)oxybenzonitrile
34		4-[4-(2-aminoethyl)phenyl]-3-[2-methyl-6-(1,3-oxazol-2-yl) pyrimidin-4-yl]oxybenzonitrile

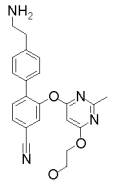
(continued)

Compound number	Structural formula	Compound name
35		4-[4-(2-aminoethyl)phenyl]-3-[2-methyl-6-(2,2,2-trifluoroethoxy) pyrimidin-4-yl]oxybenzonitrile
36		4-[4-(2-aminoethyl)phenyl]-3-[6-(3-fluoropropoxy)-2-methylpyrimidin-4-yl]oxybenzonitrile
37		4-[4-(2-aminoethyl)phenyl]-3-[2-methyl-6-(3,3,3-trifluoropropoxy) pyrimidin-4-yl]oxybenzonitrile
38		4-[4-(2-aminoethyl)phenyl]-3-(6-butoxy-2-methylpyrimidin-4-yl) oxybenzonitrile
39		4-[4-(2-aminoethyl)phenyl]-3-[6-(cyclohexylmethoxy)-2-methylpyrimidin-4-yl]oxybenzonitrile
40		4-[4-(2-aminoethyl)phenyl]-3-[2-methyl-6-(1,3-thiazol-2-yl) pyrimidin-4-yl]oxybenzonitrile

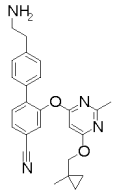
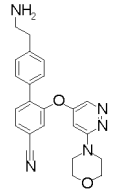
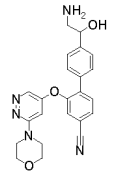
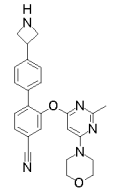
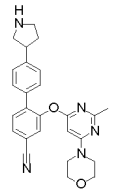
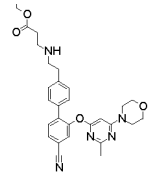
[Table 1-6]

Compound number	Structural formula	Compound name
41		4-[4-(2-aminoethyl)phenyl]-3-[2-methyl-6-(3-methylbutoxy)pyrimidin-4-yl] oxybenzonitrile
42		4-[4-(2-aminoethyl)phenyl]-3-[6-(3,3-dimethylbutoxy)-2-methylpyrimidin-4-yl] oxybenzonitrile
43		4-[4-(2-aminoethyl)phenyl]-3-[6-(cyclobutylmethoxy)-2-methylpyrimidin-4-yl] oxybenzonitrile
44		4-[4-(2-aminoethyl)phenyl]-3-[6-(cyclopentylmethoxy)-2-methylpyrimidin-4-yl] oxybenzonitrile
45		4-[4-(2-aminoethyl)phenyl]-3-(6-cyclopentyloxy-2-methylpyrimidin-4-yl) oxybenzonitrile
46		4-[4-(2-aminoethyl)phenyl]-3-(6-cyclopentyl-2-methylpyrimidin-4-yl) oxybenzonitrile
47		4-[4-(2-aminoethyl)phenyl]-3-[6-(2,2-dimethylpropoxy)-2-methylpyrimidin-4-yl] oxybenzonitrile

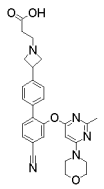
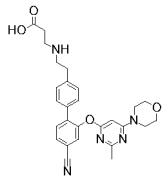
(continued)

Compound number	Structural formula	Compound name
48		4-[4-(2-aminoethyl)phenyl]-3-[6-(2-methoxyethoxy)-2-methylpyrimidin-4-yl] oxybenzonitrile

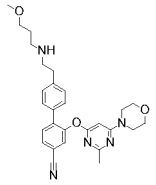
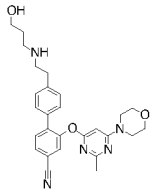
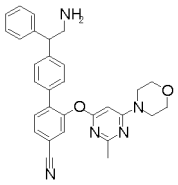
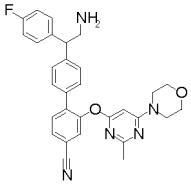
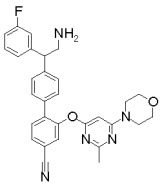
[Table 1-7]

Compound number	Structural formula	Compound name
49		4-[4-(2-aminoethyl)phenyl]-3-[2-methyl-6-[(1-methylcyclopropyl) methoxy]pyrimidi n-4-yl]oxybenzonitrile
50		4-[4-(2-aminoethyl)phenyl]-3-(6-morpholin-4-ylpyridazin-4-yl) oxybenzonitrile
51		4-[4-(2-amino-1-hydroxyethyl)phenyl]-3-(6-morpholin-4-ylpyridazin-4-yl)oxybenzonitrile
52		4-[4-(azetidin-3-yl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
53		3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxy-4-(4-pyrrolidin-3 -ylphenyl)benzonitrile
54		ethyl 3-[2-[4-[4-cyano-2-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl) oxyphenyl]phenyl]ethylamino]prop anoate

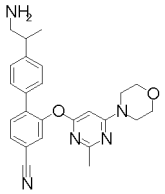
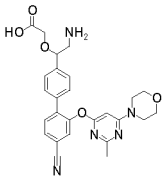
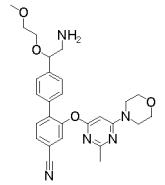
(continued)

Compound number	Structural formula	Compound name
55		3-[3-[4-[4-cyano-2-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl) oxyphenyl]phenyl]azetidin-1-yl]propanoic acid
56		3-[2-[4-[4-cyano-2-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl) oxyphenyl]phenyl]ethylamino]prop anoic acid

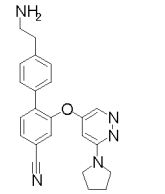
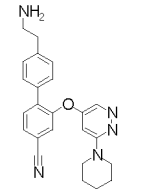
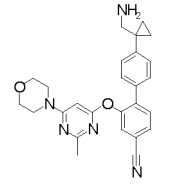
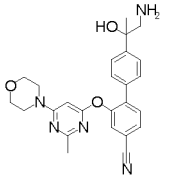
[Table 1-8]

Compound number	Structural formula	Compound name
57		4-[4-[2-(3-methoxypropylamino)ethyl]phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
58		4-[4-[2-(3-hydroxypropylamino)ethyl]phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
59		4-[4-(2-amino-1-phenylethyl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
60		4-[4-[2-amino-1-(4-fluorophenyl)ethyl]phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
61		4-[4-[2-amino-1-(3-fluorophenyl)ethyl]phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile

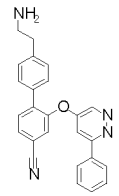
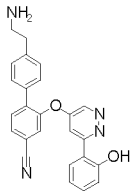
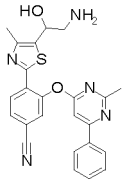
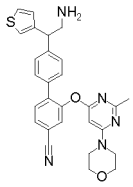
(continued)

Compound number	Structural formula	Compound name
62		4-[4-(1-aminopropan-2-yl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
63		2-[2-amino-1-[4-[4-cyano-2-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl) oxyphenyl]phenyl]ethoxy]acetic acid
64		4-[4-[2-amino-1-(2-methoxyethoxy)ethyl]phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile

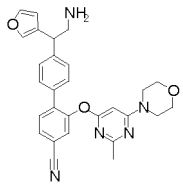
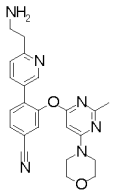
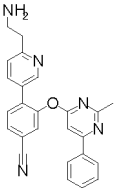
[Table 1-9]

Compound number	Structural formula	Compound name
65		4-[4-(2-aminoethyl)phenyl]-3-(6-pyrrolidin-1-ylpyridazin-4-yl) oxybenzonitrile
66		4-[4-(2-aminoethyl)phenyl]-3-(6-piperidin-1 -ylpyridazin-4-yl) oxybenzonitrile
67		4-[4-[1-(aminomethyl)cyclopropyl]phenyl]-3 - (2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
68		4-[4-(1-amino-2-hydroxypropan-2-yl)phenyl]-3 -(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile

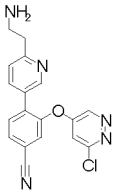
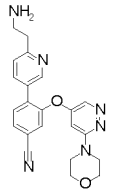
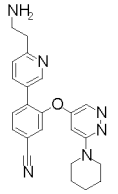
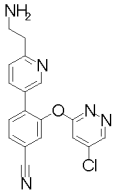
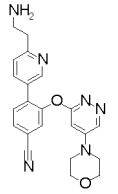
(continued)

Compound number	Structural formula	Compound name
69		4-[4-(2-aminoethyl)phenyl]-3-(6-phenylpyridazin-4-yl)oxybenzonitrile
70		4-[4-(2-aminoethyl)phenyl]-3-[6-(2-hydroxyphenyl)pyridazin-4-yl] oxybenzonitrile
71		4-[5-(2-amino-1-hydroxyethyl)-4-methyl-1,3-thiazol-2-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile
72		4-[4-(2-amino-1-thiophen-3 - ylethyl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile

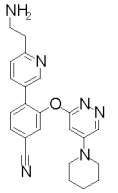
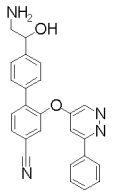
[Table 1-10]

Compound number	Structural formula	Compound name
73		4-[4-[2-amino-1-(furan-3 - yl)ethyl]phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
74		4-[6-(2-aminoethyl)pyridin-3-yl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
75		4-[6-(2-aminoethyl)pyridin-3-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl) oxybenzonitrile

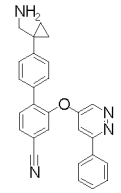
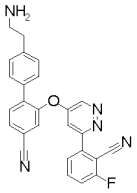
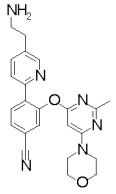
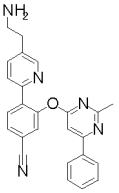
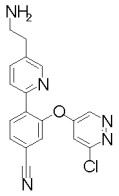
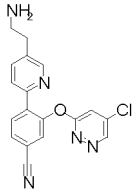
(continued)

Compound number	Structural formula	Compound name
76		4-[6-(2-aminoethyl)pyridin-3-yl]-3-(6-chloropyridazin-4-yl) oxybenzonitrile
77		4-[6-(2-aminoethyl)pyridin-3-yl]-3-(6-morpholin-4-ylpyridazin-4-yl) oxybenzonitrile
78		4-[6-(2-aminoethyl)pyridin-3-yl]-3-(6-piperidin-1 -ylpyridazin-4-yl) oxybenzonitrile
79		4-[6-(2-aminoethyl)pyridin-3-yl]-3-(5-chloropyridazin-3-yl) oxybenzonitrile
80		4-[6-(2-aminoethyl)pyridin-3-yl]-3-(5-morpholin-4-ylpyridazin-3-yl) oxybenzonitrile

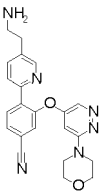
[Table 1-11]

Compound number	Structural formula	Compound name
81		4-[6-(2-aminoethyl)pyridin-3-yl]-3-(5-piperidin-1-ylpyridazin-3- yl) oxybenzonitrile
82		4-[4-(2-amino-1-hydroxyethyl)phenyl]-3-(6-phenylpyridazin-4-yl) oxybenzonitrile

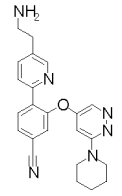
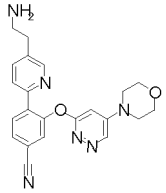
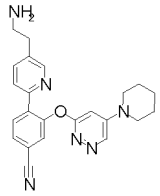
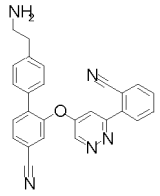
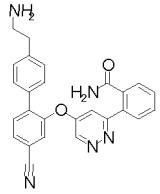
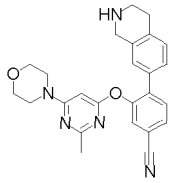
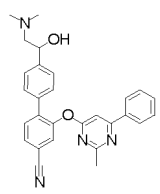
(continued)

Compound number	Structural formula	Compound name
83		4-[4-[1-(aminomethyl)cyclopropyl]phenyl]-3- (6-phenylpyridazin-4-yl) oxybenzonitrile
84		2-[5-[2-[4-(2-aminoethyl)phenyl]-5-cyanophenoxy]pyridazin-3-yl]-6-fluorobenzonitrile
85		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
86		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl) oxybenzonitrile
87		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(6-chloropyridazin-4-yl) oxybenzonitrile
88		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(5-chloropyridazin-3-yl) oxybenzonitrile

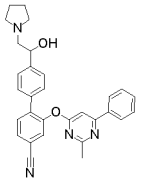
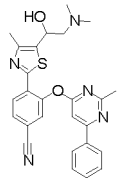
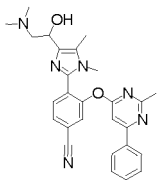
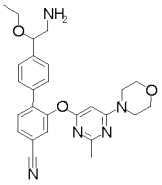
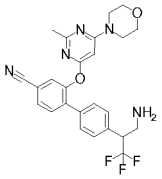
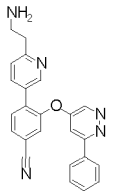
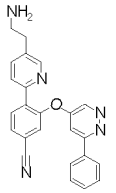
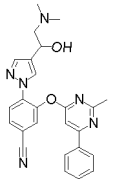
[Table 1-12]

Compound number	Structural formula	Compound name
89		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(6-morpholin-4-ylpyridazin-4-yl) oxybenzonitrile

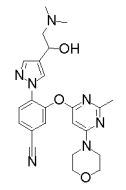
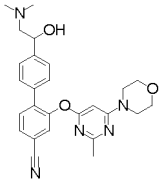
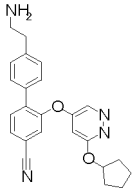
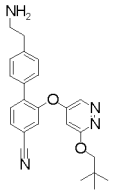
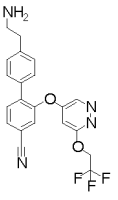
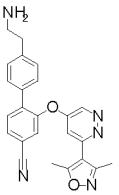
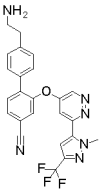
(continued)

Compound number	Structural formula	Compound name
90		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(6-piperidin-1-ylpyridazin-4-yl) oxybenzonitrile
91		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(5-morpholin-4-ylpyridazin-3-yl) oxybenzonitrile
92		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(5-piperidin-1-ylpyridazin-3-yl) oxybenzonitrile
93		4-[4-(2-aminoethyl)phenyl]-3-[6-(2-cyanophenyl)pyridazin-4-yl] oxybenzonitrile
94		2-[5-[2-[4-(2-aminoethyl)phenyl]-5-cyanophenoxy]pyridazin-3-yl] benzamide
95		3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxy-4-(1,2,3,4-tetrahydroisoquinolin-7-yl)benzonitrile
96		4-[4-[2-(dimethylamino)-1- hydroxyethyl]phenyl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile

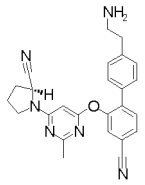
[Table 1-13]

Compound number	Structural formula	Compound name
97		4-[4-(1-hydroxy-2-pyrrolidin-1- ylethyl)phenyl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile
98		4-[5-[2-(dimethylamino)-1-hydroxyethyl]-4-methyl-1,3-thiazol-2-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile
99		4-[4-[2-(dimethylamino)-1- hydroxyethyl]-1,5-dimethylimidazol-2-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile
100		4-[4-(2-amino-1-ethoxyethyl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
101		4-[4-(3-amino-1,1,1-trifluoropropan-2-yl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
102		4-[6-(2-aminoethyl)pyridin-3-yl]-3-(6-phenylpyridazin-4-yl) oxybenzonitrile
103		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(6-phenylpyridazin-4-yl) oxybenzonitrile
104		4-[4-[2-(dimethylamino)-1-hydroxyethyl]pyrazol-1-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile

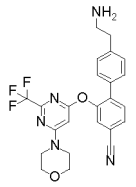
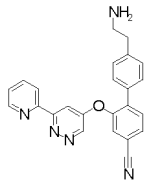
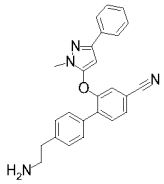
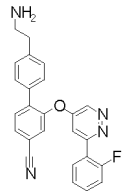
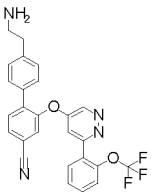
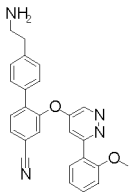
[Table 1-14]

Compound number	Structural formula	Compound name
105		4-[4-[2-(dimethylamino)-1- hydroxyethyl]pyrazol-1-yl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
106		4-[4-[2-(dimethylamino)-1- hydroxyethyl]phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
107		4-[4-(2-aminoethyl)phenyl]-3-(6-cyclopentyloxypyridazin-4-yl) oxybenzonitrile
108		4-[4-(2-aminoethyl)phenyl]-3-[6-(2,2-dimethylpropoxy)pyridazin-4-yl] oxybenzonitrile
109		4-[4-(2-aminoethyl)phenyl]-3-[6-(2,2,2-trifluoroethoxy)pyridazin-4-yl] oxybenzonitrile
110		4-[4-(2-aminoethyl)phenyl]-3-[6-(3,5-dimethyl-1,2-oxazol-4-yl)pyridazin-4-yl]oxybenzonitrile
111		4-[4-(2-aminoethyl)phenyl]-3-[6-[2-methyl-5-(trifluoromethyl)pyrazol-3-yl]pyridazin-4-yl]oxybenzonitrile

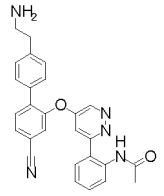
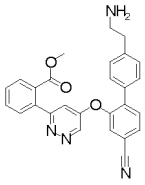
(continued)

Compound number	Structural formula	Compound name
112		(2S)-1-[6-[2-[4-(2-aminoethyl)phenyl]-5-cyanophenoxy]-2-methylpyrimidin-4-yl]pyrrolidine-2-carbonitrile

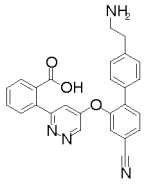
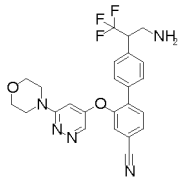
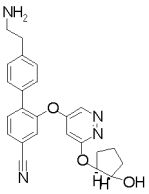
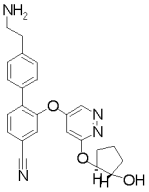
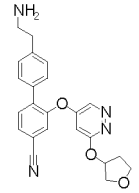
[Table 1-15]

Compound number	Structural formula	Compound name
113		4-[4-(2-aminoethyl)phenyl]-3-[6-morpholin-4-yl-2-(trifluoromethyl)pyrimidin-4-yl]oxybenzonitrile
114		4-[4-(2-aminoethyl)phenyl]-3-(6-pyridin-2-ylpyridazin-4-yl)oxybenzonitrile
115		4-[4-(2-aminoethyl)phenyl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
116		4-[4-(2-aminoethyl)phenyl]-3-[6-(2-fluorophenyl)pyridazin-4-yl] oxybenzonitrile
117		4-[4-(2-aminoethyl)phenyl]-3-[6-[2-(trifluoromethoxy)phenyl]pyridazin-4-yl] oxybenzonitrile
118		4-[4-(2-aminoethyl)phenyl]-3-[6-(2-methoxyphenyl)pyridazin-4-yl] oxybenzonitrile

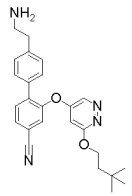
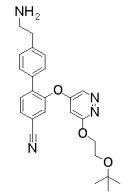
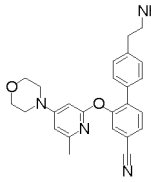
(continued)

Compound number	Structural formula	Compound name
119		N-[2-[5-[2-[4-(2-aminoethyl)phenyl]-5-cyanophenoxy]pyridazin-3-yl]phenyl] acetamide
120		methyl 2-[5-[2-[4-(2-aminoethyl)phenyl]-5-cyanophenoxy]pyridazin-3-yl] benzoate

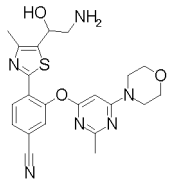
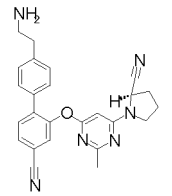
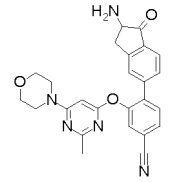
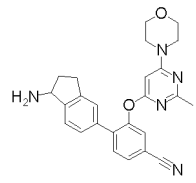
[Table 1-16]

Compound number	Structural formula	Compound name
121		2-[5-[2-[4-(2-aminoethyl)phenyl]-5-cyanophenoxy]pyridazin-3-yl] benzoic acid
122		4-[4-(3-amino-1,1,1-trifluoropropan-2-yl)phenyl]-3-(6-morpholin-4-ylpyridazin-4-yl)oxybenzonitrile
123		4-[4-(2-aminoethyl)phenyl]-3-[6-[(1S,2R)-2-hydroxycyclopentyl] oxypyridazin-4-yl]oxybenzonitrile
124		4-[4-(2-aminoethyl)phenyl]-3-[6-[(1S,2S)-2-hydroxycyclopentyl] oxypyridazin-4-yl]oxybenzonitrile
125		4-[4-(2-aminoethyl)phenyl]-3-[6-(oxolan-3-yloxy)pyridazin-4-yl] oxybenzonitrile

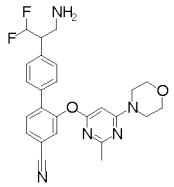
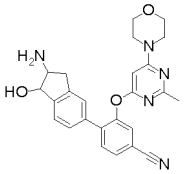
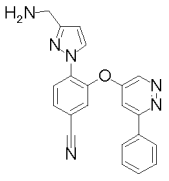
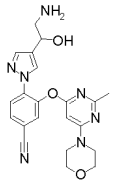
(continued)

Compound number	Structural formula	Compound name
126		4-[4-(2-aminoethyl)phenyl]-3-[6-(3,3-dimethylbutoxy)pyridazin-4-yl] oxybenzonitrile
127		4-[4-(2-aminoethyl)phenyl]-3-[6-[2-[(2-methylpropan-2-yl)oxy]ethoxy] pyridazin-4-yl]oxybenzonitrile
128		4-[4-(2-aminoethyl)phenyl]-3-(6-methyl-4-morpholin-4-ylpyridin-2-yl) oxybenzonitrile

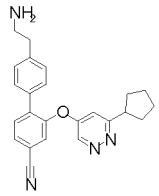
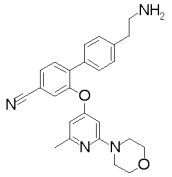
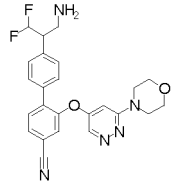
[Table 1-17]

Compound number	Structural formula	Compound name
129		4-[5-(2-amino-1-hydroxyethyl)-4-methyl-1,3-thiazol-2-yl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
130		(2R)-1-[6-[2-[4-(2-aminoethyl)phenyl]-5-cyanophenoxy]-2-methylpyrimidin-4-yl]pyrrolidine-2-carbonitrile
131		4-(2-amino-1-oxo-2,3 -dihydroinden-5-yl)-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
132		4-(1-amino-2,3-dihydro-1H-inden-5- yl)-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile

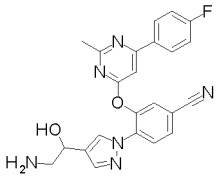
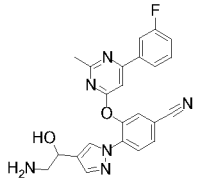
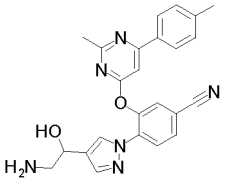
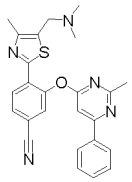
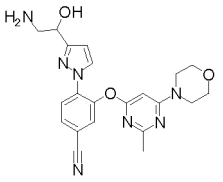
(continued)

Compound number	Structural formula	Compound name
133		4-[4-(3-amino-1,1-difluoropropan-2-yl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
134		4-(2-amino-1-hydroxy-2,3-dihydro-1H-inden-5-yl)-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
135		4-[3-(aminomethyl)pyrazol-1-yl]-3-(6-phenylpyridazin-4-yl) oxybenzonitrile
136		4-[4-(2-amino-1-hydroxyethyl)pyrazol-1-yl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile

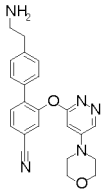
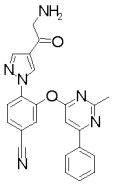
[Table 1-18]

Compound number	Structural formula	Compound name
137		4-[4-(2-aminoethyl)phenyl]-3-(6-cyclopentylpyridazin-4-yl) oxybenzonitrile
138		4-[4-(2-aminoethyl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
139		4-[4-(3-amino-1,1-difluoropropan-2-yl)phenyl]-3-(6-morpholin-4-ylpyridazin-4-yl)oxybenzonitrile

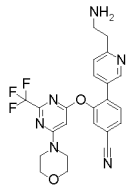
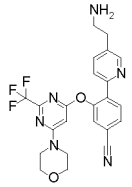
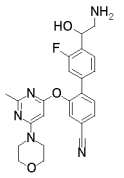
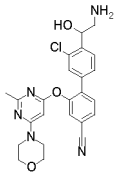
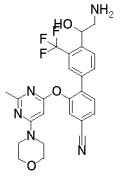
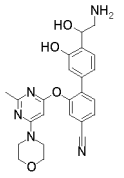
(continued)

Compound number	Structural formula	Compound name
140		4-[4-(2-amino-1-hydroxyethyl)pyrazol-1-yl]-3-[6-(4-fluorophenyl)-2-methylpyrimidin-4-yl]oxybenzonitrile
141		4-[4-(2-amino-1-hydroxyethyl)pyrazol-1-yl]-3-[6-(3-fluorophenyl)-2-methylpyrimidin-4-yl]oxybenzonitrile
142		4-[4-(2-amino-1-hydroxyethyl)pyrazol-1-yl]-3-[2-methyl-6-(4-methylphenyl)pyrimidin-4-yl]oxybenzonitrile
143		4-[5-[(dimethylamino)methyl]-4-methyl-1,3-thiazol-2-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile
144		4-[3-(2-amino-1-hydroxyethyl)pyrazol-1-yl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile

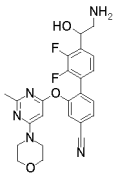
[Table 1-19]

Compound number	Structural formula	Compound name
145		4-[4-(2-aminoethyl)phenyl]-3-(5-morpholin-4-ylpyridazin-3- yl) oxybenzonitrile
146		4-[4-(2-aminoacetyl)pyrazol-1-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl) oxybenzonitrile

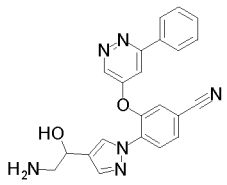
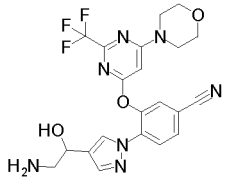
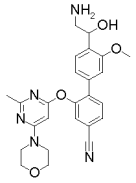
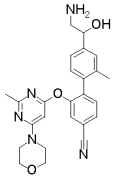
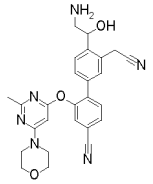
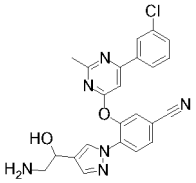
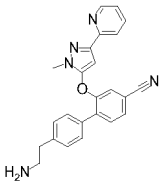
(continued)

Compound number	Structural formula	Compound name
147		4-[6-(2-aminoethyl)pyridin-3-yl]-3-[6-morpholin-4-yl-2-(trifluoromethyl) pyrimidin-4-yl]oxybenzonitrile
148		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[6-morpholin-4-yl-2-(trifluoromethyl) pyrimidin-4-yl]oxybenzonitrile
149		4-[4-(2-amino-1-hydroxyethyl)-3-fluorophenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
150		4-[4-(2-amino-1-hydroxyethyl)-3-chlorophenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
151		4-[4-(2-amino-1-hydroxyethyl)-3-(trifluoromethyl)phenyl] -3 -(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
152		4-[4-(2-amino-1-hydroxyethyl)-3-hydroxyphenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile

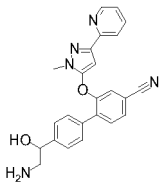
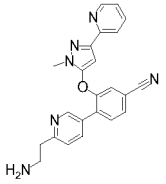
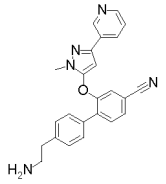
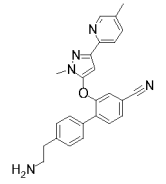
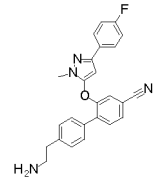
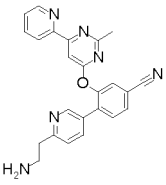
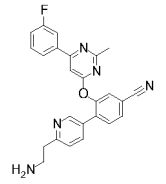
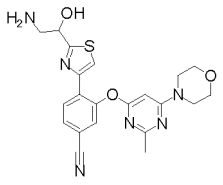
[Table 1-20]

Compound number	Structural formula	Compound name
153		4-[4-(2-amino-1-hydroxyethyl)-2,3-difluorophenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile

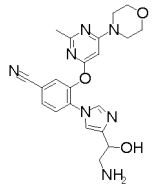
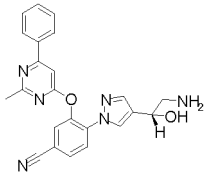
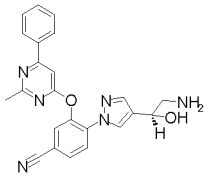
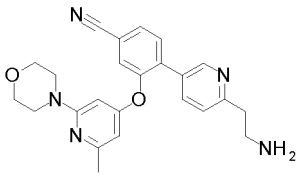
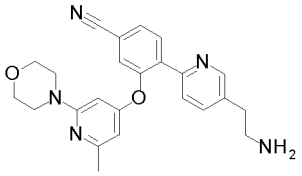
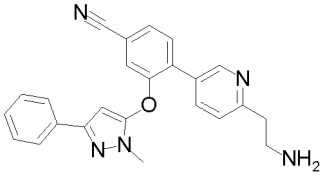
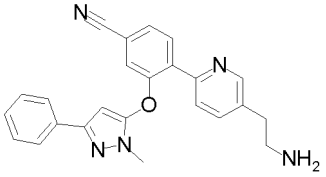
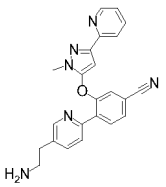
(continued)

Compound number	Structural formula	Compound name
154		4-[4-(2-amino-1-hydroxyethyl)pyrazol-1-yl]-3-(6-phenylpyridazin-4-yl)oxybenzonitrile
155		4-[4-(2-amino-1-hydroxyethyl)pyrazol-1-yl]-3-[6-morpholin-4-yl-2-(trifluoromethyl)pyrimidin-4-yl]oxybenzonitrile
156		4-[4-(2-amino-1-hydroxyethyl)-3-methoxyphenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
157		4-[4-(2-amino-1-hydroxyethyl)-2-methylphenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
158		4-[4-(2-amino-1-hydroxyethyl)-3-(cyanomethyl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
159		4-[4-(2-amino-1-hydroxyethyl)pyrazol-1-yl]-3-[6-(3-chlorophenyl)-2-methylpyrimidin-4-yl]oxybenzonitrile
160		4-[4-(2-aminoethyl)phenyl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile

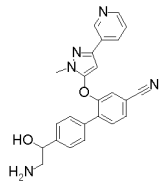
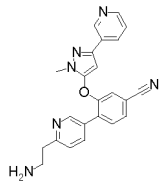
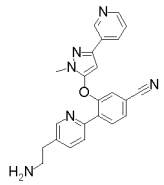
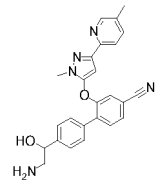
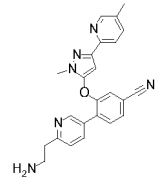
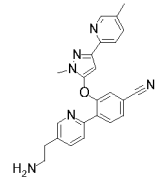
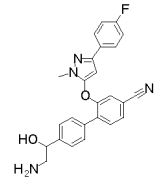
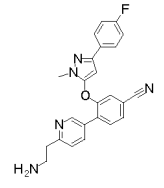
[Table 1-21]

Compound number	Structural formula	Compound name
161		4-[4-(2-amino-1-hydroxyethyl)phenyl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3 - yl)oxybenzonitrile
162		4-[6-(2-aminoethyl)pyridin-3-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
163		4-[4-(2-aminoethyl)phenyl]-3-(2-methyl-5-pyridin-3-ylpyrazol-3-yl) oxybenzonitrile
164		4-[4-(2-aminoethyl)phenyl]-3-[2-methyl-5-(5-methylpyridin-2-yl) pyrazol-3 -yl]oxybenzonitrile
165		4-[4-(2-aminoethyl)phenyl]-3-[5-(4-fluorophenyl)-2-methylpyrazol-3 - yl]oxybenzonitrile
166		4-[6-(2-aminoethyl)pyridin-3-yl]-3-(2-methyl-6-pyridin-2-ylpyrimidin-4-yl)oxybenzonitrile
167		4-[6-(2-aminoethyl)pyridin-3-yl]-3-[6-(3-fluorophenyl)-2-methylpyrimidin-4-yl]oxybenzonitrile
168		4-[2-(2-amino-1-hydroxyethyl)-1,3-thiazol-4-yl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile

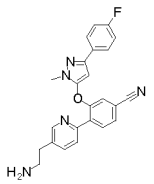
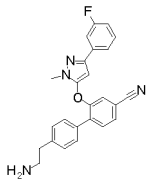
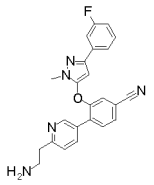
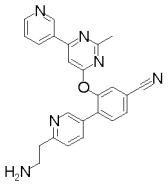
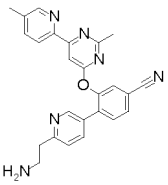
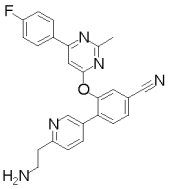
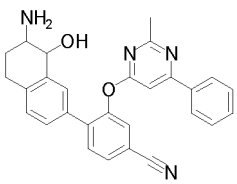
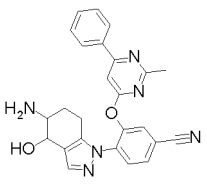
[Table 1-22]

Compound number	Structural formula	Compound name
169		4-[4-(2-amino-1-hydroxyethyl)imidazol-1-yl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
170		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile
171		4-[4-[(1S)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile
172		4-[6-(2-aminoethyl)pyridin-3-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
173		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
174		4-[6-(2-aminoethyl)pyridin-3-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
175		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
176		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile

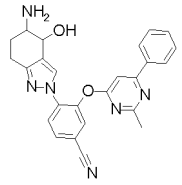
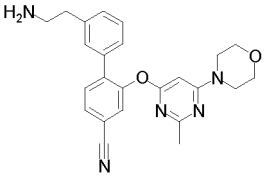
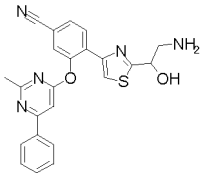
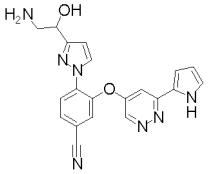
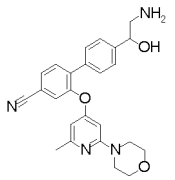
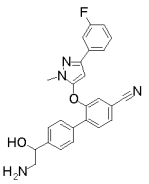
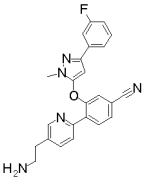
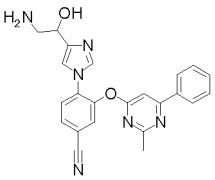
[Table 1-23]

Compound number	Structural formula	Compound name
177		4-[4-(2-amino-1-hydroxyethyl)phenyl]-3-(2-methyl-5-pyridin-3 -ylpyrazol-3- yl)oxybenzonitrile
178		4-[6-(2-aminoethyl)pyridin-3-yl]-3-(2-methyl-5-pyridin-3-ylpyrazol-3-yl)oxybenzonitrile
179		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-5-pyridin-3-ylpyrazol-3-yl)oxybenzonitrile
180		4-[4-(2-amino-1-hydroxyethyl)phenyl]-3-[2-methyl-5-(5-methylpyridin-2-yl)pyrazol-3-yl]oxybenzonitrile
181		4-[6-(2-aminoethyl)pyridin-3-yl]-3-[2-methyl-5-(5-methylpyridin-2-yl) pyrazol-3-yl]oxybenzonitrile
182		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-methyl-5-(5-methylpyridin-2-yl) pyrazol-3 -yl]oxybenzonitrile
183		4-[4-(2-amino-1-hydroxyethyl)phenyl]-3-[5-(4-fluorophenyl)-2-methylpyrazol-3 - yl]oxybenzonitrile
184		4-[6-(2-aminoethyl)pyridin-3-yl]-3-[5-(4-fluorophenyl)-2-methylpyrazol-3-yl]oxybenzonitrile

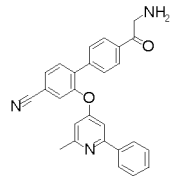
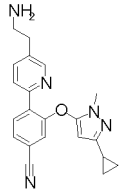
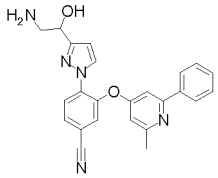
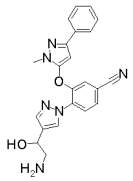
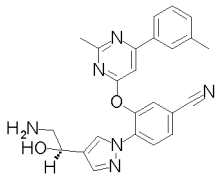
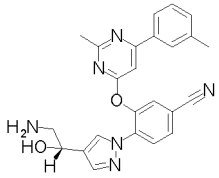
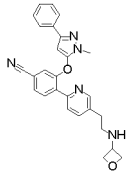
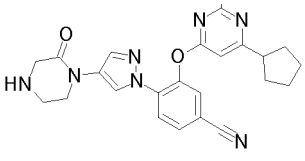
[Table 1-24]

Compound number	Structural formula	Compound name
185		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[5-(4-fluorophenyl)-2-methylpyrazol-3-yl]oxybenzonitrile
186		4-[4-(2-aminoethyl)phenyl]-3-[5-(3-fluorophenyl)-2-methylpyrazol-3 - yl]oxybenzonitrile
187		4-[6-(2-aminoethyl)pyridin-3-yl]-3-[5-(3 -fluorophenyl)-2-methylpyrazol-3-yl]oxybenzonitrile
188		4-[6-(2-aminoethyl)pyridin-3-yl]-3-(2-methyl-6-pyridin-3-ylpyrimidin-4-yl)oxybenzonitrile
189		4-[6-(2-aminoethyl)pyridin-3-yl]-3-[2-methyl-6-(5-methylpyridin-2-yl)pyrimidin-4-yl]oxybenzonitrile
190		4-[6-(2-aminoethyl)pyridin-3-yl]-3-[6-(4-fluorophenyl)-2-methylpyrimidin-4-yl]oxybenzonitrile
191		4-(7-amino-8-hy droxy-5,6,7,8-tetrahydronaphthalen-2-yl)-3 -(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile
192		4-(5-amino-4-hydroxy-4,5,6,7-tetrahydroindazol-1-yl)-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile

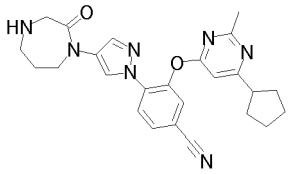
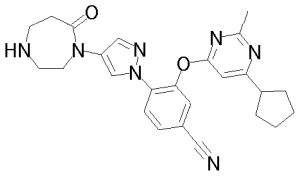
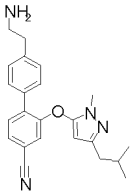
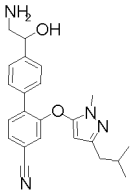
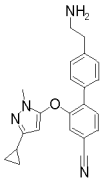
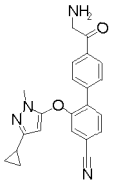
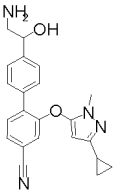
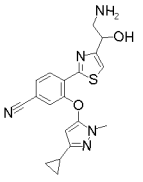
[Table 1-25]

Compound number	Structural formula	Compound name
193		4-(5-amino-4-hydroxy-4,5,6,7-tetrahydroindazol-2-yl)-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile
194		4-[3-(2-aminoethyl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
195		4-[2-(2-amino-1-hydroxyethyl)-1,3-thiazol-4-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile
196		4-[3-(2-amino-1-hydroxyethyl)pyrazol-1-yl]-3-[6-(1H-pyrrol-2-yl)pyridazin-4-yl]oxybenzonitrile
197		4-[4-(2-amino-1-hydroxyethyl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
198		4-[4-(2-amino-1-hydroxyethyl)phenyl]-3-[5-(3-fluorophenyl)-2-methylpyrazol-3 - yl]oxybenzonitrile
199		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[5-(3-fluorophenyl)-2-methylpyrazol-3-yl]oxybenzonitrile
200		4-[4-(2-amino-1-hydroxyethyl)imidazol-1-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile

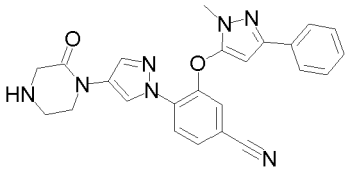
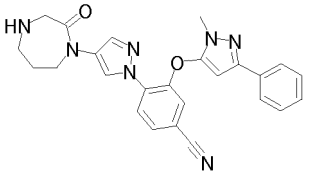
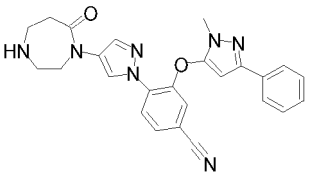
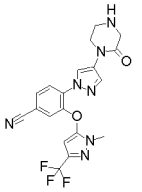
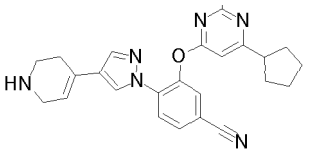
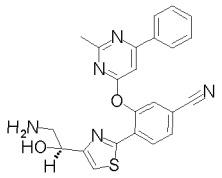
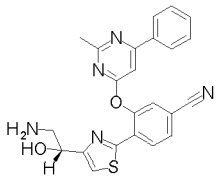
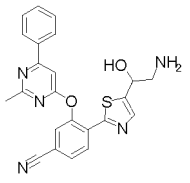
[Table 1-26]

Compound number	Structural formula	Compound name
201		4-[4-(2-aminoacetyl)phenyl]-3-(2-methyl-6-phenylpyridin-4-yl)oxybenzonitrile
202		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3 - yl)oxybenzonitrile
203		4-[3-(2-amino-1-hydroxyethyl)pyrazol-1-yl]-3-(2-methyl-6-phenylpyridin-4-yl)oxybenzonitrile
204		4-[4-(2-amino-1-hydroxyethyl)pyrazol-1-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
205		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[2-methyl-6-(3-methylphenyl)pyrimidin-4-yl]oxybenzonitrile
206		4-[4-[(1S)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[2-methyl-6-(3-methylphenyl)pyrimidin-4-yl]oxybenzonitrile
207		3-(2-methyl-5-phenylpyrazol-3- yl)oxy-4-[5-[2-(oxetan-3-ylamino)ethyl]pyridin-2-yl]benzonitrile
208		3-(6-cyclopentyl-2-methylpyrimidin-4-yl)oxy-4-[4-(2-oxopiperazin-1-yl)pyrazol-1-yl]benzonitrile

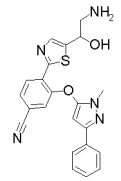
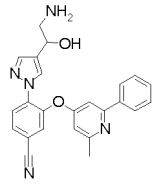
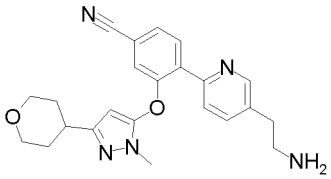
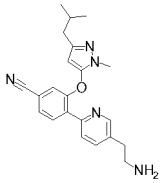
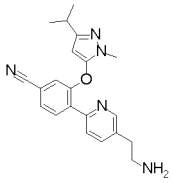
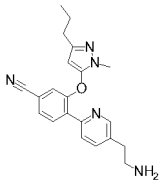
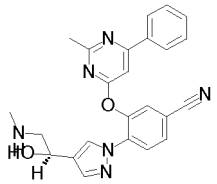
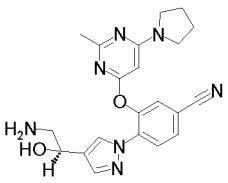
[Table 1-27]

Compound number	Structural formula	Compound name
209		3-(6-cyclopentyl-2-methylpyrimidin-4-yl)oxy-4-[4-(2-oxo-1,4-diazepan-1-yl)pyrazol-1-yl]benzonitrile
210		3-(6-cyclopentyl-2-methylpyrimidin-4-yl)oxy-4-[4-(7-oxo-1,4-diazepan-1-yl)pyrazol-1-yl]benzonitrile
211		4-[4-(2-aminoethyl)phenyl]-3-[2-methyl-5-(2-methylpropyl) pyrazol-3-yl]oxybenzonitrile
212		4-[4-(2-amino-1-hydroxyethyl)phenyl]-3-[2-methyl-5-(2-methylpropyl)pyrazol-3-yl]oxybenzonitrile
213		4-[4-(2-aminoethyl)phenyl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
214		4-[4-(2-aminoacetyl)phenyl]-3-(5 - cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
215		4-[4-(2-amino-1-hydroxyethyl)phenyl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
216		4-[4-(2-amino-1-hydroxyethyl)-1,3-thiazol-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile

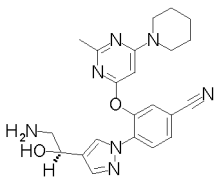
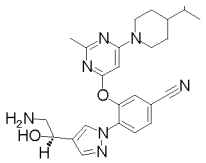
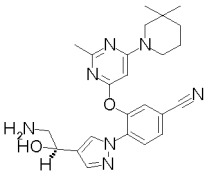
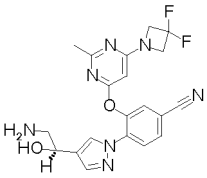
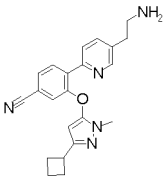
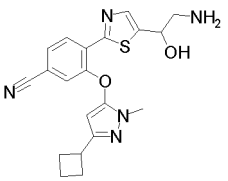
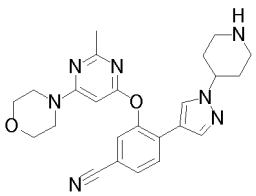
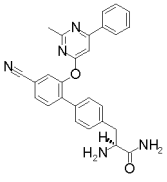
[Table 1-28]

Compound number	Structural formula	Compound name
217		3-(2-methyl-5-phenylpyrazol-3- yl)oxy-4-[4-(2-oxopiperazin-1- yl)pyrazol-1-yl]benzonitrile
218		3-(2-methyl-5-phenylpyrazol-3- yl)oxy-4-[4-(2-oxo-1,4-diazepan-1-yl)pyrazol-1-yl]benzonitrile
219		3-(2-methyl-5-phenylpyrazol-3- yl)oxy-4-[4-(7-oxo-1,4-diazepan-1-yl)pyrazol-1-yl]benzonitrile
220		3-[2-methyl-5-(trifluoromethyl)pyrazol-3-yl]oxy-4-[4-(2-oxopiperazin-1-yl)pyrazol-1-yl]benzonitrile
221		3-(6-cyclopentyl-2-methylpyrimidin-4-yl)oxy-4-[4-(1,2,3,6-tetrahydropyridin-4-yl)pyrazol-1- yl] benzonitrile
222		4-[4-[(1S)-2-amino-1-hydroxyethyl]-1,3-thiazol-2-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile
223		4-[4-[(1R)-2-amino-1-hydroxyethyl]-1,3 -thiazol-2-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile
224		4-[5-(2-amino-1-hydroxyethyl)-1,3-thiazol-2-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile

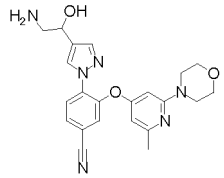
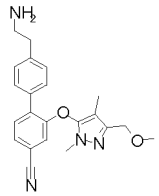
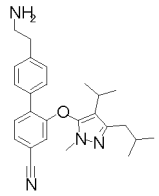
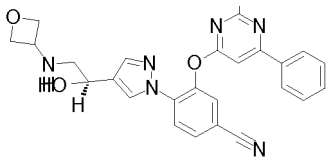
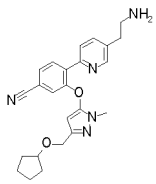
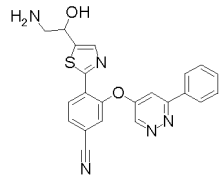
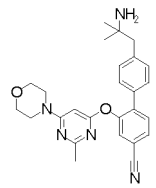
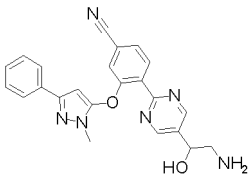
[Table 1-29]

Compound number	Structural formula	Compound name
225		4-[5-(2-amino-1-hydroxyethyl)-1,3-thiazol-2-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
226		4-[4-(2-amino-1-hydroxyethyl)pyrazol-1-yl]-3-(2-methyl-6-phenylpyridin-4-yl)oxybenzonitrile
227		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl]oxybenzonitrile
228		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-methyl-5-(2-methylpropyl)pyrazol-3-yl]oxybenzonitrile
229		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxybenzonitrile
230		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-propylpyrazol-3 - yl)oxybenzonitrile
231		4-[4-[(1R)-1-hydroxy-2-(methylamino)ethyl]pyrazol-1-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile
232		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-(2-methyl-6-pyrrolidin-1-ylpyrimidin-4-yl)oxybenzonitrile

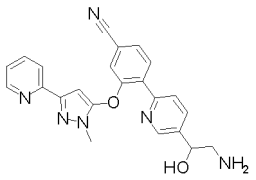
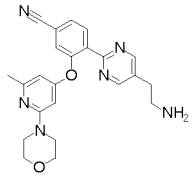
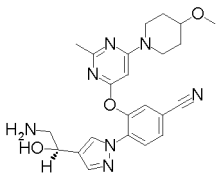
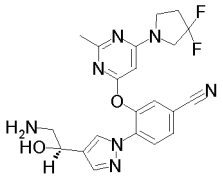
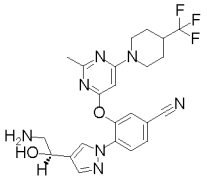
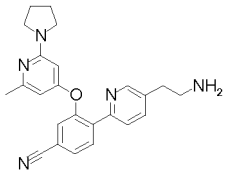
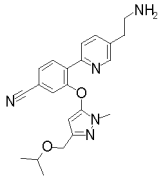
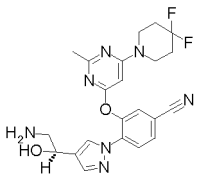
[Table 1-30]

Compound number	Structural formula	Compound name
233		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-(2-methyl-6-piperidin-1-ylpyrimidin-4-yl)oxybenzonitrile
234		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[2-methyl-6-(4-propan-2-ylpiperidin-1-yl)pyrimidin-4-yl]oxybenzonitrile
235		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[6-(3,3-dimethylpiperidin-1-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile
236		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[6-(3,3-difluoroazetidin-1-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile
237		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(5-cyclobutyl-2-methylpyrazol-3 - yl)oxybenzonitrile
238		4-[5-(2-amino-1-hydroxyethyl)-1,3-thiazol-2-yl]-3-(5-cyclobutyl-2-methylpyrazol-3-yl)oxybenzonitrile
239		3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxy-4-(1-piperidin-4-ylpyrazol-4-yl)benzonitrile
240		(2S)-2-amino-3-[4-[4-cyano-2-(2-methyl-6-phenylpyrimidin-4-yl)oxyphenyl]phenyl]propanamide

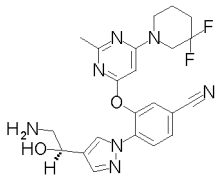
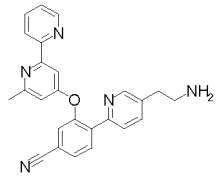
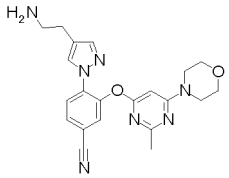
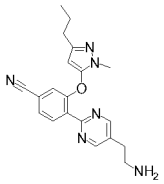
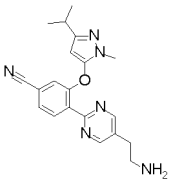
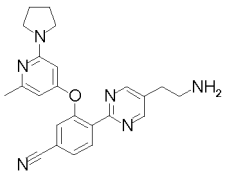
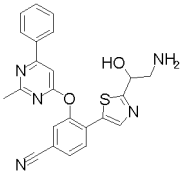
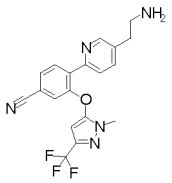
[Table 1-31]

Compound number	Structural formula	Compound name
241		4-[4-(2-amino-1-hydroxyethyl)pyrazol-1-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
242		4-[4-(2-aminoethyl)phenyl]-3-[5-(methoxymethyl)-2,4-dimethylpyrazol-3-yl]oxybenzonitrile
243		4-[4-(2-aminoethyl)phenyl]-3-[2-methyl-5-(2-methylpropyl)-4-propan-2-ylpyrazol-3-yl]oxybenzonitrile
244		4-[4-[(1R)-1-hydroxy-2-(oxetan-3-ylamino)ethyl]pyrazol-1-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile
245		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[5-(cyclopentyloxymethyl)-2-methylpyrazol-3-yl]oxybenzonitrile
246		4-[5-(2-amino-1-hydroxyethyl)-1,3-thiazol-2-yl]-3-(6-phenylpyridazin-4-yl)oxybenzonitrile
247		4-[4-(2-amino-2-methylpropyl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
248		4-[5-(2-amino-1-hydroxyethyl)pyrimidin-2-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile

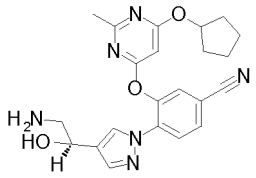
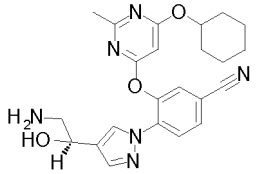
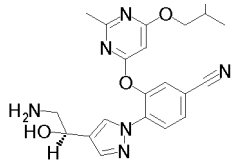
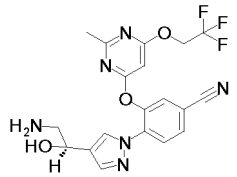
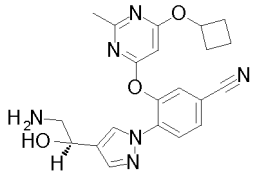
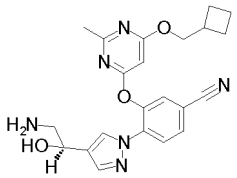
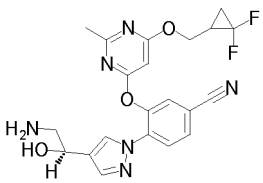
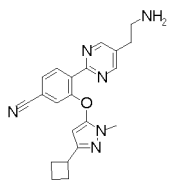
[Table 1-32]

Compound number	Structural formula	Compound name
249		4-[5-(2-amino-1-hydroxyethyl)pyridin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
250		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
251		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[6-(4-methoxypiperidin-1-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile
252		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[6-(3,3-difluoropyrrolidin-1-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile
253		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[2-methyl-6-[4-(trifluoromethyl)piperidin-1-yl]pyrimidin-4-yl] oxybenzonitrile
254		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-6-pyrrolidin-1-ylpyridin-4-yl)oxybenzonitrile
255		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-methyl-5-(propan-2-yloxymethyl)pyrazol-3- yl]oxybenzonitrile
256		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[6-(4,4-difluoropiperidin-1-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile

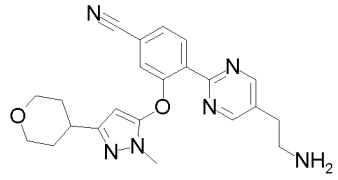
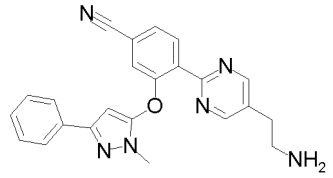
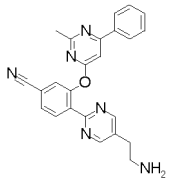
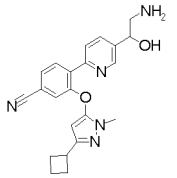
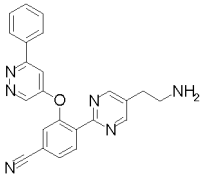
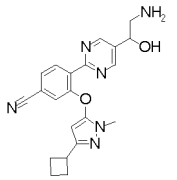
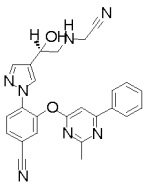
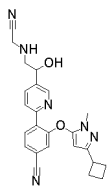
[Table 1-33]

Compound number	Structural formula	Compound name
257		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[6-(3,3-difluoropiperidin-1-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile
258		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-6-pyridin-2-ylpyridin-4-yl)oxybenzonitrile
259		4-[4-(2-aminoethyl)pyrazol-1-yl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
260		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-propylpyrazol-3-yl)oxybenzonitrile
261		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxybenzonitrile
262		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-pyrrolidin-1-ylpyridin-4-yl)oxybenzonitrile
263		4-[2-(2-amino-1-hydroxyethyl)-1,3-thiazol-5-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile
264		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-methyl-5-(trifluoromethyl)pyrazol-3-yl]oxybenzonitrile

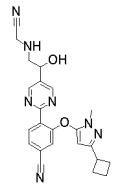
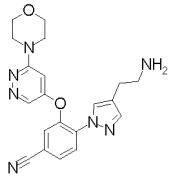
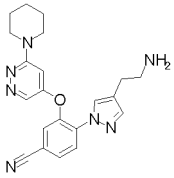
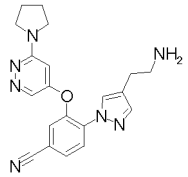
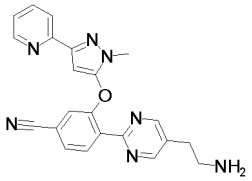
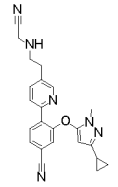
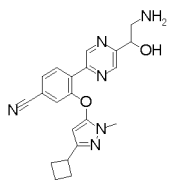
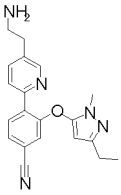
[Table 1-34]

Compound number	Structural formula	Compound name
265		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-(6-cyclopentyloxy-2-methylpyrimidin-4-yl)oxybenzonitrile
266		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-(6-cyclohexyloxy-2-methylpyrimidin-4-yl)oxybenzonitrile
267		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[2-methyl-6-(2-methylpropoxy)pyrimidin-4-yl]oxybenzonitrile
268		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[2-methyl-6-(2,2,2-trifluoroethoxy)pyrimidin-4-yl]oxybenzonitrile
269		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-(6-cyclobutyloxy-2-methylpyrimidin-4-yl)oxybenzonitrile
270		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[6-(cyclobutylmethoxy)-2-methylpyrimidin-4-yl]oxybenzonitrile
271		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[6-[(2,2-difluorocyclopropyl)methoxy]-2-methylpyrimidin-4-yl] oxybenzonitrile
272		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-cyclobutyl-2-methylpyrazol-3 - yl)oxybenzonitrile

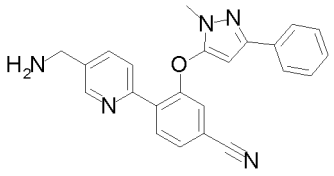
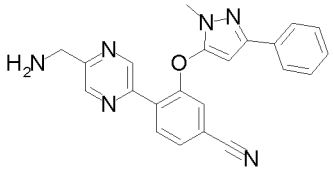
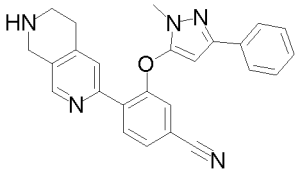
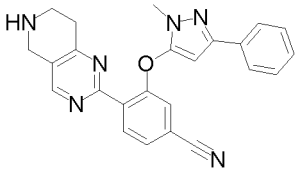
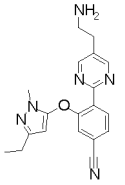
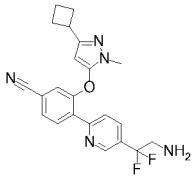
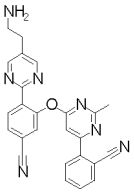
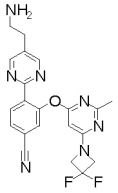
[Table 1-35]

Compound number	Structural formula	Compound name
273		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-(oxan-4-yl) pyrazol-3-yl]oxybenzonitrile
274		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
275		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile
276		4-[5-(2-amino-1-hydroxyethyl)pyridin-2-yl]-3-(5-cyclobutyl-2-methylpyrazol-3 - yl)oxybenzonitrile
277		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(6-phenylpyridazin-4-yl) oxybenzonitrile
278		4-[5-(2-amino-1-hydroxyethyl)pyrimidin-2-yl]-3-(5-cyclobutyl-2-methylpyrazol-3 - yl)oxybenzonitrile
279		4-[4-[(1R)-2-(cyanomethylamino)-1-hydroxyethyl]pyrazol-1-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile
280		4-[5-[2-(cyanomethylamino)-1-hydroxyethyl]pyridin-2-yl]-3-(5-cyclobutyl-2-methylpyrazol-3 - yl)oxybenzonitrile

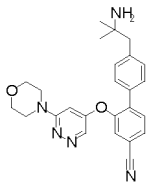
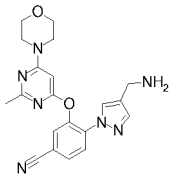
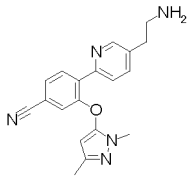
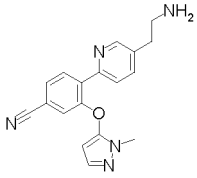
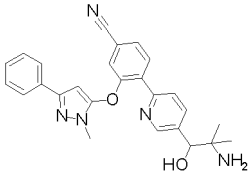
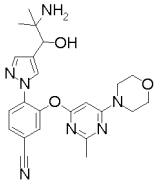
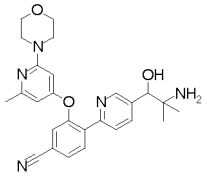
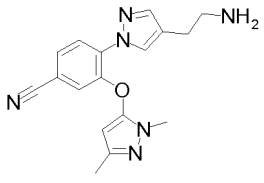
[Table 1-36]

Compound number	Structural formula	Compound name
281		4-[5-[2-(cyanomethylamino)-1-hydroxyethyl]pyrimidin-2-yl]-3-(5-cyclobutyl-2-methylpyrazol-3 - yl)oxybenzonitrile
282		4-[4-(2-aminoethyl)pyrazol-1-yl]-3-(6-morpholin-4-ylpyridazin-4-yl) oxybenzonitrile
283		4-[4-(2-aminoethyl)pyrazol-1-yl]-3-(6-piperidin-1-ylpyridazin-4-yl) oxybenzonitrile
284		4-[4-(2-aminoethyl)pyrazol-1-yl]-3-(6-pyrrolidin-1-ylpyridazin-4-yl) oxybenzonitrile
285		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
286		4-[5-[2-(cyanomethylamino)ethyl]pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3 -yl)oxybenzonitrile
287		4-[5-(2-amino-1-hydroxyethyl)pyrazin-2-yl]-3-(5-cyclobutyl-2-methylpyrazol-3- yl)oxybenzonitrile
288		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(5-ethyl-2-methylpyrazol-3- yl) oxybenzonitrile

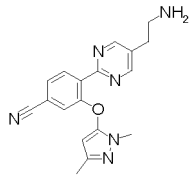
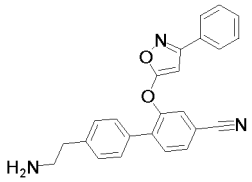
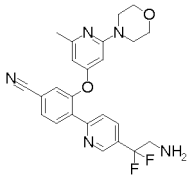
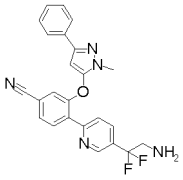
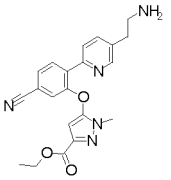
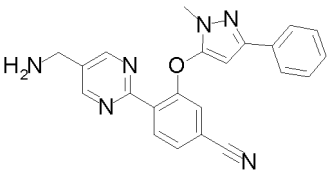
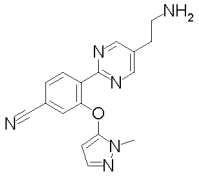
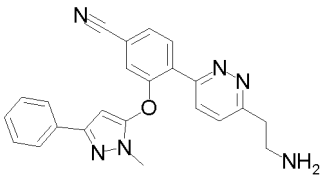
[Table 1-37]

Compound number	Structural formula	Compound name
289		4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
290		4-[5-(aminomethyl)pyrazin-2-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
291		3-(2-methyl-5-phenylpyrazol-3- yl)oxy-4-(5, 6,7, 8-tetrahydro-2,7-naphthylidin-3-yl)benzonitrile
292		3-(2-methyl-5-phenylpyrazol-3- yl)oxy-4-(5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-2-yl)benzonitrile
293		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-ethyl-2-methylpyrazol-3- yl)oxybenzonitrile
294		4-[5-(2-amino-1,1-difluoroethyl)pyridin-2-yl]-3-(5-cyclobutyl-2-methylpyrazol-3- yl)oxybenzonitrile
295		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[6-(2-cyanophenyl)-2-methylpyrimidin-4-yl]oxybenzonitrile
296		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[6-(3,3-difluoroazetidin-1-yl)-2-methylpyrimidin-4-yl] oxybenzonitrile

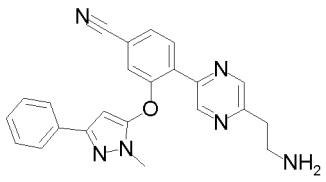
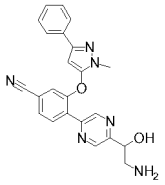
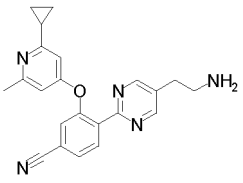
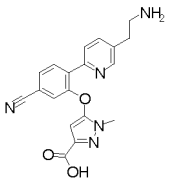
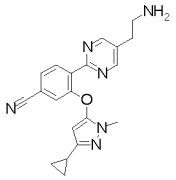
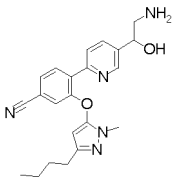
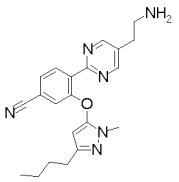
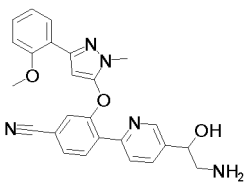
[Table 1-38]

Compound number	Structural formula	Compound name
297		4-[4-(2-amino-2-methylpropyl)phenyl]-3-(6-morpholin-4-ylpyridazin-4-yl)oxybenzonitrile
298		4-[4-(aminomethyl)pyrazol-1-yl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
299		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2,5-dimethylpyrazol-3- yl) oxybenzonitrile
300		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methylpyrazol-3-yl) oxybenzonitrile
301		4-[5-(2-amino-1-hydroxy-2-methylpropyl)pyridin-2-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
302		4-[4-(2-amino-1-hydroxy-2-methylpropyl)pyrazol-1-yl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
303		4-[5-(2-amino-1-hydroxy-2-methylpropyl)pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
304		4-[4-(2-aminoethyl)pyrazol-1-yl]-3-(2,5-dimethylpyrazol-3- yl) oxybenzonitrile

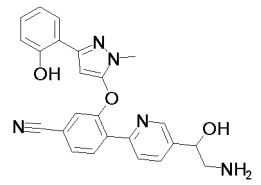
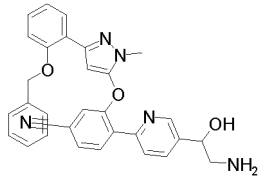
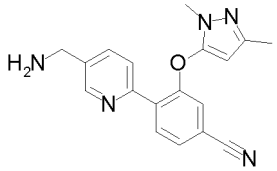
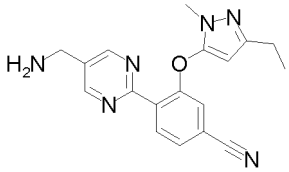
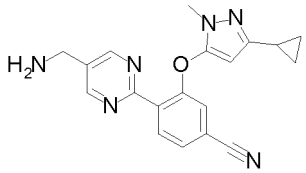
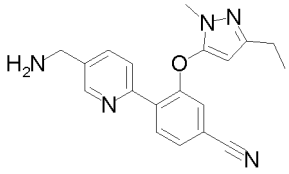
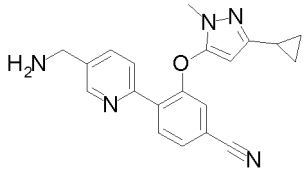
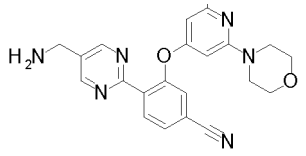
[Table 1-39]

Compound number	Structural formula	Compound name
305		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2,5-dimethylpyrazol-3- yl)oxybenzonitrile
306		4-[4-(2-aminoethyl)phenyl]-3-[(3-phenyl-1,2-oxazol-5-yl)oxy]benzonitrile
307		4-[5-(2-amino-1,1-difluoroethyl)pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
308		4-[5-(2-amino-1,1-difluoroethyl)pyridin-2-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
309		ethyl 5-[2-[5-(2-aminoethyl)pyridin-2-yl]-5-cyanophenoxy]-1-methylpyrazole-3-carboxylate
310		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
311		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methylpyrazol-3-yl)oxybenzonitrile
312		4-[6-(2-aminoethyl)pyridazin-3-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile

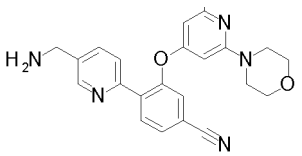
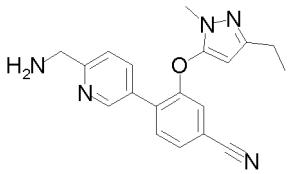
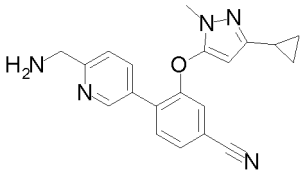
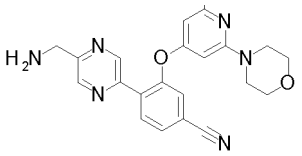
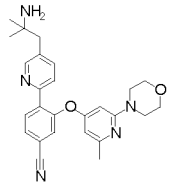
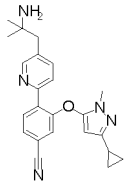
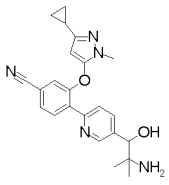
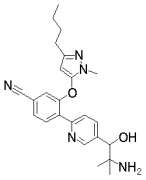
[Table 1-40]

Compound number	Structural formula	Compound name
313		4-[5-(2-aminoethyl)pyrazin-2-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
314		4-[5-(2-amino-1-hydroxyethyl)pyrazin-2-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
315		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-cyclopropyl-6-methylpyridin-4-yl)oxybenzonitrile
316		5-[2-[5-(2-aminoethyl)pyridin-2-yl]-5-cyanophenoxy]-1-methylpyrazole-3-carboxylic acid
317		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3 - yl)oxybenzonitrile
318		4-[5-(2-amino-1-hydroxyethyl)pyridin-2-yl]-3-(5-butyl-2-methylpyrazol-3-yl)oxybenzonitrile
319		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-butyl-2-methylpyrazol-3-yl)oxybenzonitrile
320		4-[5-(2-amino-1-hydroxyethyl)pyridin-2-yl]-3-[5-(2-methoxyphenyl)-2-methylpyrazol-3 - yl]oxybenzonitrile

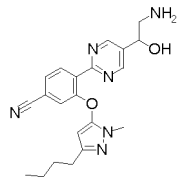
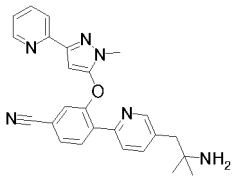
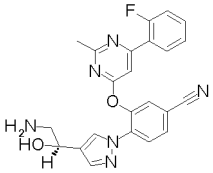
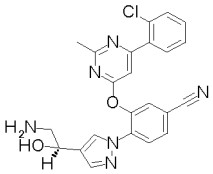
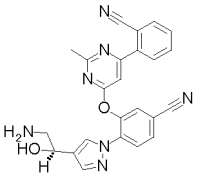
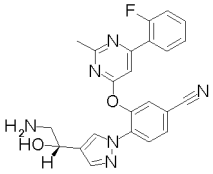
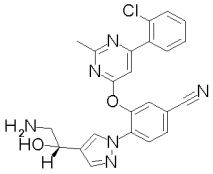
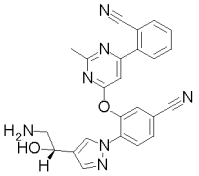
[Table 1-41]

Compound number	Structural formula	Compound name
321		4-[5-(2-amino-1-hydroxyethyl)pyridin-2-yl]-3-[5-(2-hydroxyphenyl)-2-methylpyrazol-3 - yl]oxybenzonitrile
322		4-[5-(2-amino-1-hydroxyethyl)pyridin-2-yl]-3-[2-methyl-5-(2-phenylmethoxyphenyl)pyrazol-3-yl]oxybenzonitrile
323		4-[5-(aminomethyl)pyridin-2-yl]-3-(2,5-dimethylpyrazol-3 - yl) oxybenzonitrile
324		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(5 -ethyl -2-methylpyrazol-3- yl)oxybenzonitrile
325		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
326		4-[5-(aminomethyl)pyridin-2-yl]-3-(5-ethyl-2-methylpyrazol-3-yl)oxybenzonitrile
327		4-[5-(aminomethyl)pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
328		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile

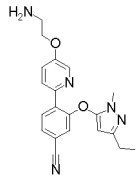
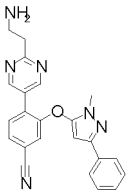
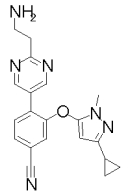
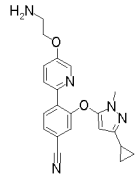
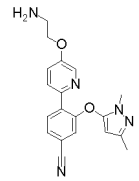
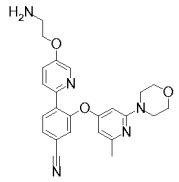
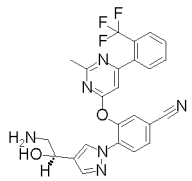
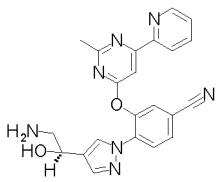
[Table 1-42]

Compound number	Structural formula	Compound name
329		4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
330		4-[6-(aminomethyl)pyridin-3-yl]-3-(5-ethyl-2-methylpyrazol-3- yl)oxybenzonitrile
331		4-[6-(aminomethyl)pyridin-3-yl]-3-(5-cyclopropyl-2-methylpyrazol-3- yl)oxybenzonitrile
332		4-[5-(aminomethyl)pyrazin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
333		4-[5-(2-amino-2-methylpropyl)pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
334		4-[5-(2-amino-2-methylpropyl)pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3 - yl)oxybenzonitrile
335		4-[5-(2-amino-1-hydroxy-2-methylpropyl)pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
336		4-[5-(2-amino-1-hydroxy-2-methylpropyl)pyridin-2-yl]-3-(5-butyl-2-methylpyrazol-3-yl)oxybenzonitrile

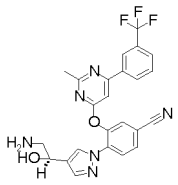
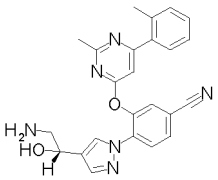
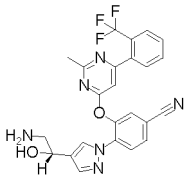
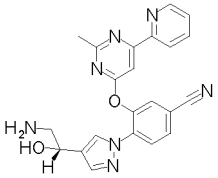
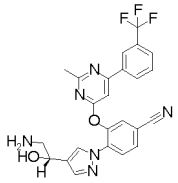
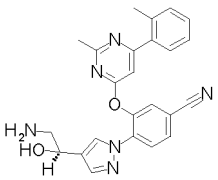
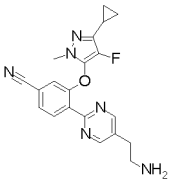
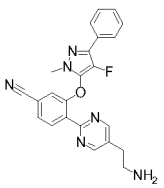
[Table 1-43]

Compound number	Structural formula	Compound name
337		4-[5-(2-amino-1-hydroxyethyl)pyrimidin-2-yl]-3-(5-butyl-2-methylpyrazol-3-yl)oxybenzonitrile
338		4-[5-(2-amino-2-methylpropyl)pyridin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
339		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[6-(2-fluorophenyl)-2-methylpyrimidin-4-yl]oxybenzonitrile
340		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[6-(2-chlorophenyl)-2-methylpyrimidin-4-yl]oxybenzonitrile
341		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[6-(2-cyanophenyl)-2-methylpyrimidin-4-yl]oxybenzonitrile
342		4-[4-[(1S)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[6-(2-fluorophenyl)-2-methylpyrimidin-4-yl]oxybenzonitrile
343		4-[4-[(1S)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[6-(2-chlorophenyl)-2-methylpyrimidin-4-yl]oxybenzonitrile
344		4-[4-[(1S)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[6-(2-cyanophenyl)-2-methylpyrimidin-4-yl]oxybenzonitrile

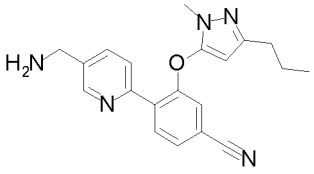
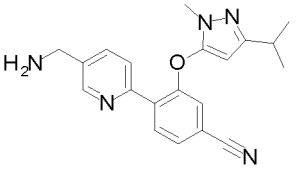
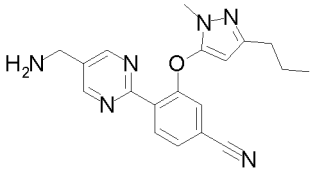
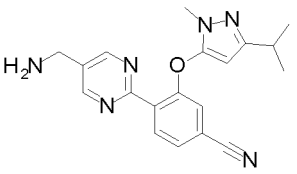
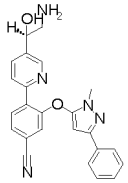
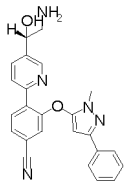
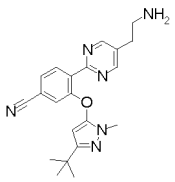
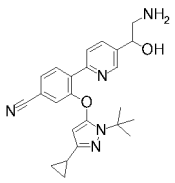
[Table 1-44]

Compound number	Structural formula	Compound name
345		4-[5-(2-aminoethoxy)pyridin-2-yl]-3-(5-ethyl-2-methylpyrazol-3- yl) oxybenzonitrile
346		4-[2-(2-aminoethyl)pyrimidin-5-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
347		4-[2-(2-aminoethyl)pyrimidin-5-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
348		4-[5-(2-aminoethoxy)pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
349		4-[5-(2-aminoethoxy)pyridin-2-yl]-3-(2,5-dimethylpyrazol-3 - yl) oxybenzonitrile
350		4-[5-(2-aminoethoxy)pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
351		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[2-methyl-6-[2-(trifluoromethyl)phenyl]pyrimidin-4-yl]oxybenzonitrile
352		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-(2-methyl-6-pyridin-2-ylpyrimidin-4-yl)oxybenzonitrile

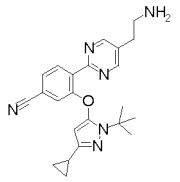
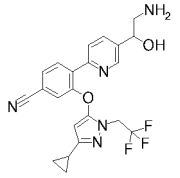
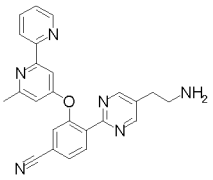
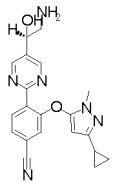
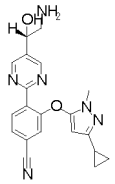
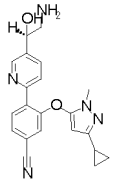
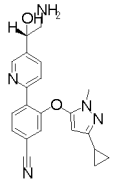
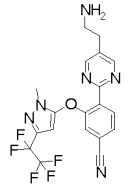
[Table 1-45]

Compound number	Structural formula	Compound name
353		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[2-methyl-6-[3-(trifluoromethyl)phenyl]pyrimidin-4-yl]oxybenzonitrile
354		4-[4-[(1S)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[2-methyl-6-(2-methylphenyl)pyrimidin-4-yl]oxybenzonitrile
355		4-[4-[(1S)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[2-methyl-6-[2-(trifluoromethyl)phenyl]pyrimidin-4-yl]oxybenzonitrile
356		4-[4-[(1S)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-(2-methyl-6-pyridin-2-ylpyrimidin-4-yl)oxybenzonitrile
357		4-[4-[(1S)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[2-methyl-6-[3-(trifluoromethyl)phenyl]pyrimidin-4-yl]oxybenzonitrile
358		4-[4-[(1R)-2-amino-1-hydroxyethyl]pyrazol-1-yl]-3-[2-methyl-6-(2-methylphenyl)pyrimidin-4-yl]oxybenzonitrile
359		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-cyclopropyl-4-fluoro-2-methylpyrazol-3-yl)oxybenzonitrile
360		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(4-fluoro-2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile

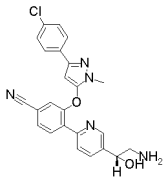
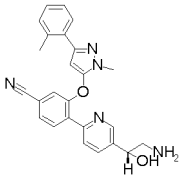
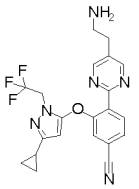
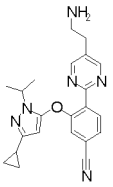
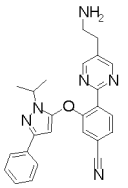
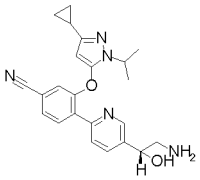
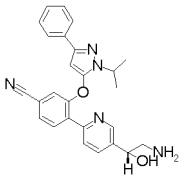
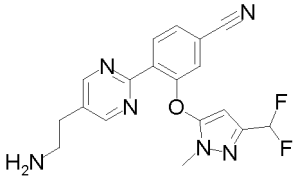
[Table 1-46]

Compound number	Structural formula	Compound name
361		4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-5-propylpyrazol-3 - yl)oxybenzonitrile
362		4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxybenzonitrile
363		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-propylpyrazol-3 - yl)oxybenzonitrile
364		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxybenzonitrile
365		4-[5-[(1R)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
366		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
367		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-tert-butyl-2-methylpyrazol-3-yl)oxybenzonitrile
368		4-[5-(2-amino-1-hydroxyethyl)pyridin-2-yl]-3-(2-tert-butyl-5-cyclopropylpyrazol-3-yl)oxybenzonitrile

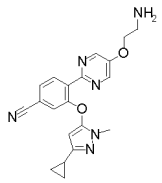
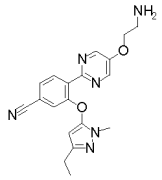
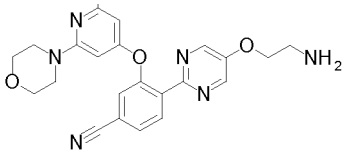
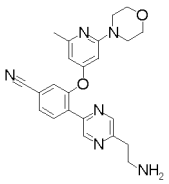
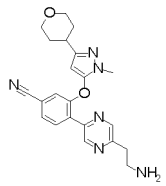
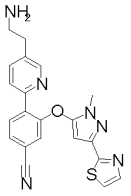
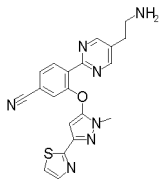
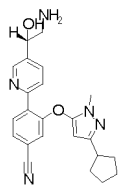
[Table 1-47]

Compound number	Structural formula	Compound name
369		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-tert-butyl-5-cyclopropylpyrazol-3 - yl)oxybenzonitrile
370		4-[5-(2-amino-1-hydroxyethyl)pyridin-2-yl]-3-[5-cyclopropyl-2-(2,2,2-trifluoroethyl)pyrazol-3-yl]oxybenzonitrile
371		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-pyridin-2-ylpyridin-4-yl)oxybenzonitrile
372		4-[5-[(1R)-2-amino-1-hydroxyethyl]pyrimidin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3 - yl)oxybenzonitrile
373		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyrimidin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
374		4-[5-[(1R)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3 - yl)oxybenzonitrile
375		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3 - yl)oxybenzonitrile
376		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-(1,1,2,2,2-pentafluoroethyl)pyrazol-3-yl]oxybenzonitrile

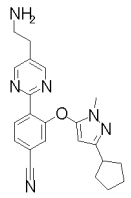
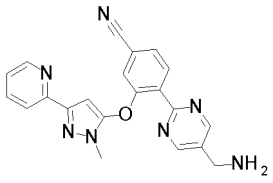
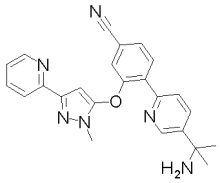
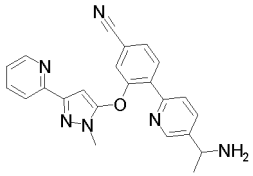
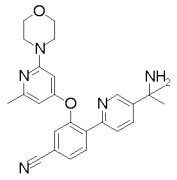
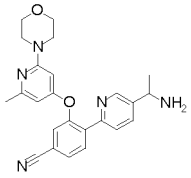
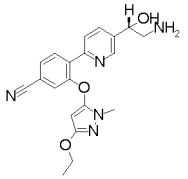
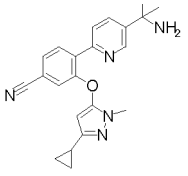
[Table 1-48]

Compound number	Structural formula	Compound name
377		4-[5-[(1R)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[5-(4-chlorophenyl)-2-methylpyrazol-3 - yl]oxybenzonitrile
378		4-[5-[(1R)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[2-methyl-5-(2-methylphenyl)pyrazol-3-yl]oxybenzonitrile
379		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-cyclopropyl-2-(2,2,2-trifluoroethyl)pyrazol-3-yl]oxybenzonitrile
380		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-cyclopropyl-2-propan-2-ylpyrazol-3-yl)oxybenzonitrile
381		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5 -phenyl -2-propan-2-ylpyrazol -3 - yl)oxybenzonitrile
382		4-[5-[(1R)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(5-cyclopropyl-2-propan-2-ylpyrazol-3-yl)oxybenzonitrile
383		4-[5-[(1R)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(5-phenyl-2-propan-2-ylpyrazol-3-yl)oxybenzonitrile
384		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-(difluoromethyl)-2-methylpyrazol-3-yl]oxybenzonitrile

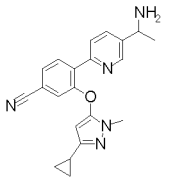
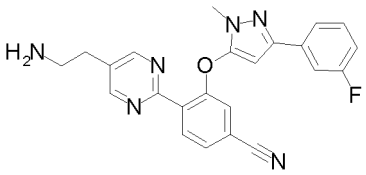
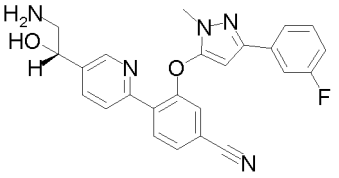
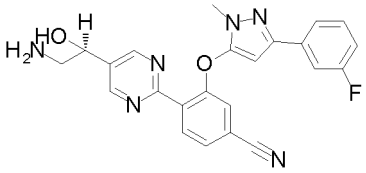
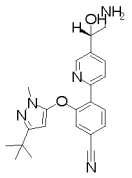
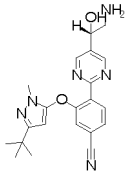
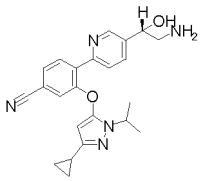
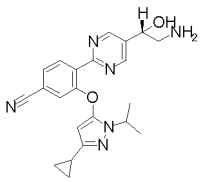
[Table 1-49]

Compound number	Structural formula	Compound name
385		4-[5-(2-aminoethoxy)pyrimidin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
386		4-[5-(2-aminoethoxy)pyrimidin-2-yl]-3-(5-ethyl-2-methylpyrazol-3-yl)oxybenzonitrile
387		4-[5-(2-aminoethoxy)pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
388		4-[5-(2-aminoethyl)pyrazin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
389		4-[5-(2-aminoethyl)pyrazin-2-yl]-3-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl]oxybenzonitrile
390		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-methyl-5-(1,3-thiazol-2-yl)pyrazol-3-yl]oxybenzonitrile
391		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-(1,3-thiazol-2-yl)pyrazol-3-yl]oxybenzonitrile
392		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(5-cyclopentyl-2-methylpyrazol-3-yl)oxybenzonitrile

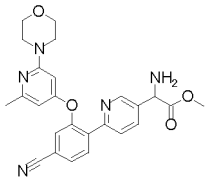
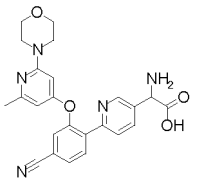
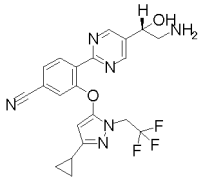
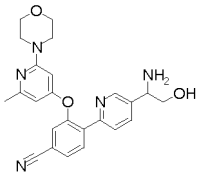
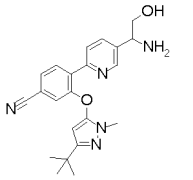
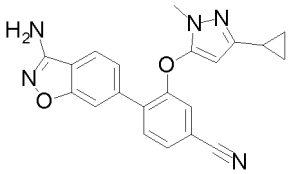
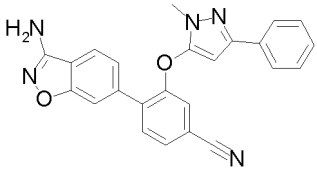
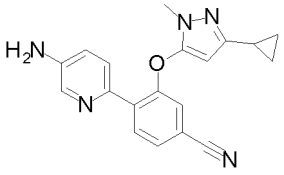
[Table 1-50]

Compound number	Structural formula	Compound name
393		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-cyclopentyl-2-methylpyrazol-3-yl)oxybenzonitrile
394		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
395		4-[5-(2-aminopropan-2-yl)pyridin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
396		4-[5-(1-aminoethyl)pyridin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
397		4-[5-(2-aminopropan-2-yl)pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
398		4-[5-(1-aminoethyl)pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
399		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(5-ethoxy-2-methylpyrazol-3- yl)oxybenzonitrile
400		4-[5-(2-aminopropan-2-yl)pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile

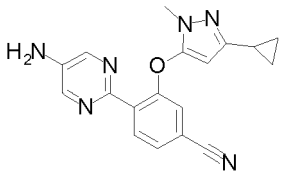
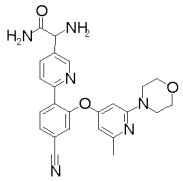
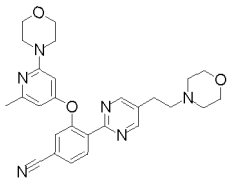
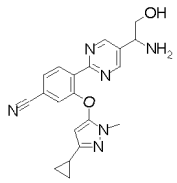
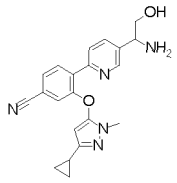
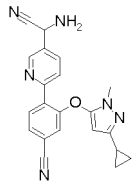
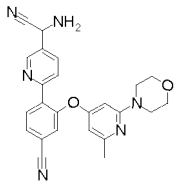
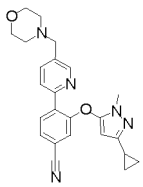
[Table 1-51]

Compound number	Structural formula	Compound name
401		4-[5-(1-aminoethyl)pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3 - yl)oxybenzonitrile
402		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-(3-fluorophenyl)-2-methylpyrazol-3-yl]oxybenzonitrile
403		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[5-(3-fluorophenyl)-2-methylpyrazol-3 - yl] oxybenzonitrile
404		4-[5-(2-amino-1-hydroxyethyl)pyrimidin-2-yl]-3-[5-(3-fluorophenyl)-2-methylpyrazol-3 - yl]oxybenzonitrile
405		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(5-tert-butyl-2-methylpyrazol-3-yl)oxybenzonitrile
406		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyrimidin-2-yl]-3-(5-tert-butyl-2-methylpyrazol-3 - yl)oxybenzonitrile
407		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(5-cyclopropyl-2-propan-2-ylpyrazol-3 - yl) oxybenzonitrile
408		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyrimidin-2-yl]-3-(5-cyclopropyl-2-propan-2-ylpyrazol-3-yl) oxybenzonitrile

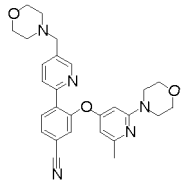
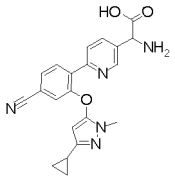
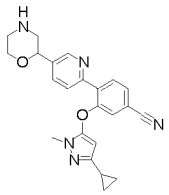
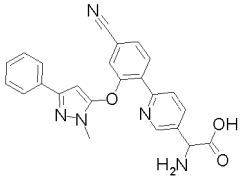
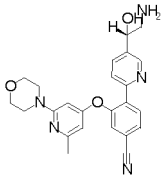
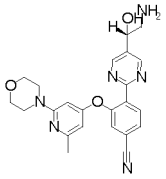
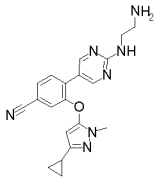
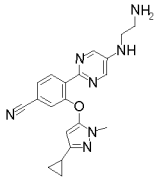
[Table 1-52]

Compound number	Structural formula	Compound name
409		methyl 2-amino-2-[6-[4-cyano-2-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxyphenyl]pyridin-3-yl]acetate
410		2-amino-2-[6-[4-cyano-2-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxyphenyl]pyridin-3-yl]acetic acid
411		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyrimidin-2-yl]-3-[5-cyclopropyl-2-(2,2,2-trifluoroethyl)pyrazol-3-yl] oxybenzonitrile
412		4-[5-(1-amino-2-hydroxyethyl)pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
413		4-[5-(1-amino-2-hydroxyethyl)pyridin-2-yl]-3-(5-tert-butyl-2-methylpyrazol-3-yl)oxybenzonitrile
414		4-(3-amino-1,2-benzoxazol-6-yl)-3 - (5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
415		4-(3-amino-1,2-benzoxazol-6-yl)-3 - (2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
416		4-(5-aminopyridin-2-yl)-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile

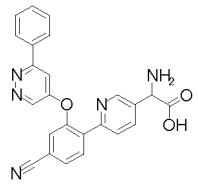
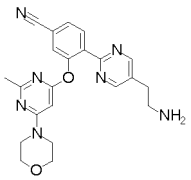
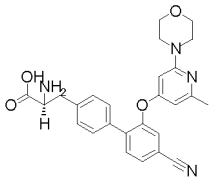
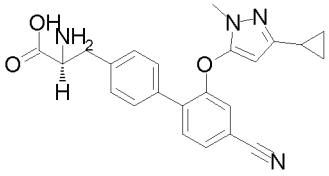
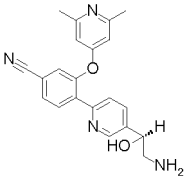
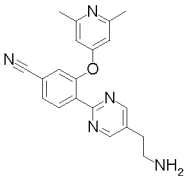
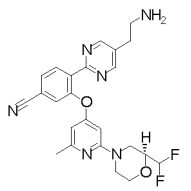
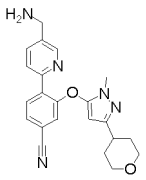
[Table 1-53]

Compound number	Structural formula	Compound name
417		4-(5-aminopyrimidin-2-yl)-3-(5 - cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
418		2-amino-2-[6-[4-cyano-2-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxyphenyl]pyridin-3-yl]acetamide
419		3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxy-4-[5-(2-morpholin-4-ylethyl)pyrimidin-2-yl]benzonitrile
420		4-[5-(1-amino-2-hydroxyethyl)pyrimidin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
421		4-[5-(1-amino-2-hydroxyethyl)pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
422		4-[5-[amino(cyano)methyl]pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
423		4-[5-[amino(cyano)methyl]pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
424		3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxy-4-[5-(morpholin-4-ylmethyl)pyridin-2-yl]benzonitrile

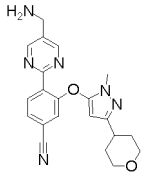
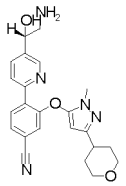
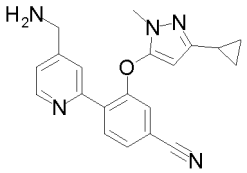
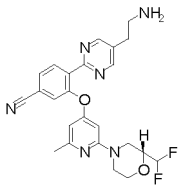
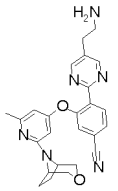
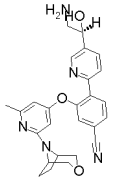
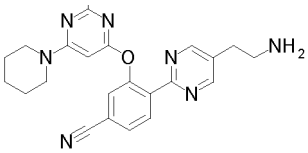
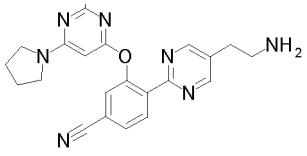
[Table 1-54]

Compound number	Structural formula	Compound name
425		3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxy-4-[5-(morpholin-4-ylmethyl)pyridin-2-yl]benzonitrile
426		2-amino-2-[6-[4-cyano-2-(5-cyclopropyl-2-methylpyrazol-3-yl) oxyphenyl]pyridin-3-yl]acetic acid
427		3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxy-4-(5-morpholin-2-ylpyridin-2-yl)benzonitrile
428		2-amino-2-[6-[4-cyano-2-(2-methyl-5-phenylpyrazol-3-yl) oxyphenyl]pyridin-3-yl]acetic acid
429		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
430		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
431		4-[2-(2-aminoethylamino)pyrimidin-5-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
432		4-[5-(2-aminoethylamino)pyrimidin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile

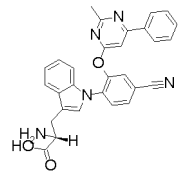
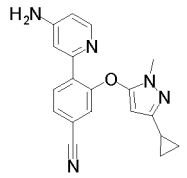
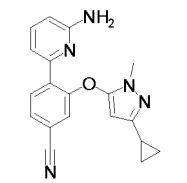
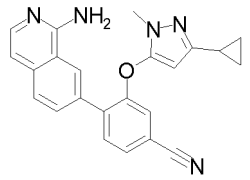
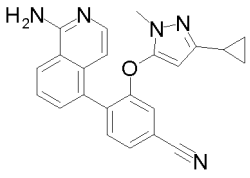
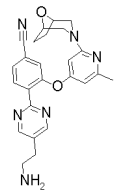
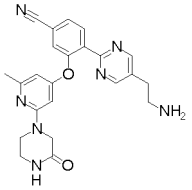
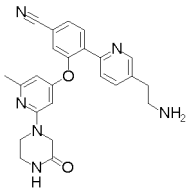
[Table 1-55]

Compound number	Structural formula	Compound name
433		2-amino-2-[6-[4-cyano-2-(6-phenylpyridazin-4-yl) oxyphenyl]pyridin-3-yl]acetic acid
434		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
435		(2S)-2-amino-3-[4-[4-cyano-2-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxyphenyl]phenyl]propanoic acid
436		(2S)-2-amino-3-[4-[4-cyano-2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxyphenyl]phenyl]propanoic acid
437		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(2,6-dimethylpyridin-4-yl)oxybenzonitrile
438		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2,6-dimethylpyridin-4-yl)oxybenzonitrile
439		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-[(2S)-2-(difluoromethyl)morpholin-4-yl]-6-methylpyridin-4-yl] oxybenzonitrile
440		4-[5-(aminomethyl)pyridin-2-yl]-3-[2-methyl-5-(oxan-4-yl) pyrazol-3-yl]oxybenzonitrile

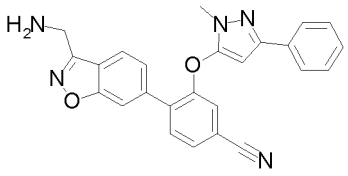
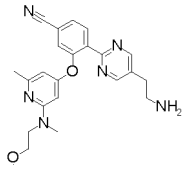
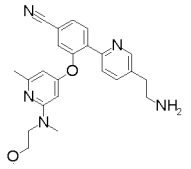
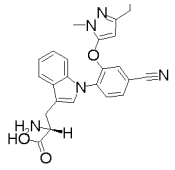
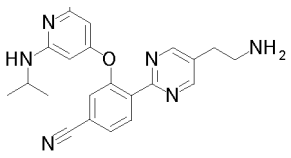
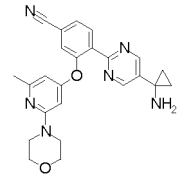
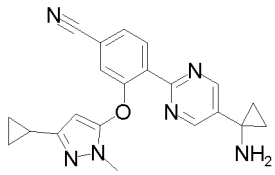
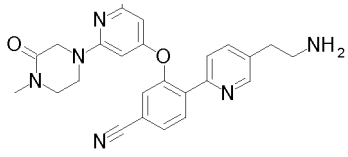
[Table 1-56]

Compound number	Structural formula	Compound name
441		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(oxan-4-yl) pyrazol-3-yl]oxybenzonitrile
442		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl]oxybenzonitrile
443		4-[4-(aminomethyl)pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3 - yl)oxybenzonitrile
444		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-[(2R)-2-(difluoromethyl) morpholin-4-yl]-6-methylpyridin-4-yl]oxybenzonitrile
445		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(3 -oxa-8-azabicyclo[3.2.1]octan-8-yl)pyridin-4-yl]oxybenzonitrile
446		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[2-methyl-6-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)pyridin-4-yl] oxybenzonitrile
447		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-piperidin-1-ylpyrimidin-4-yl)oxybenzonitrile
448		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-pyrrolidin-1 -ylpyrimidin-4-yl)oxybenzonitrile

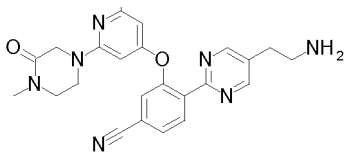
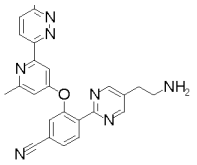
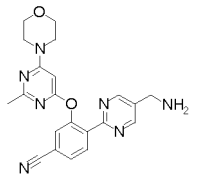
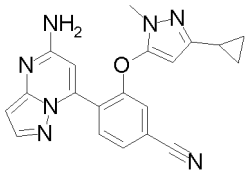
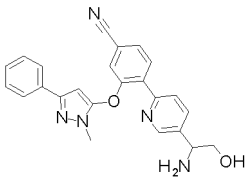
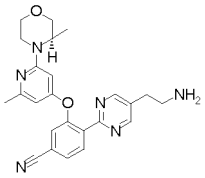
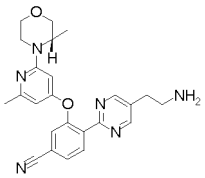
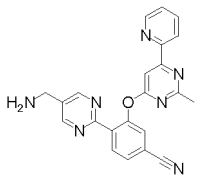
[Table 1-57]

Compound number	Structural formula	Compound name
449		2-amino-3-[1-[4-cyano-2-(2-methyl-6-phenylpyrimidin-4-yl) oxyphenyl]indol-3-yl]propanoic acid
450		4-(4-aminopyridin-2-yl)-3-(5-cyclopropyl-2-methylpyrazol-3-yl) oxybenzonitrile
451		4-(6-aminopyridin-2-yl)-3-(5-cyclopropyl-2-methylpyrazol-3-yl) oxybenzonitrile
452		4-(1-aminoisoquinolin-7-yl)-3-(5-cyclopropyl-2-methylpyrazol-3 - yl)oxybenzonitrile
453		4-(1-aminoisoquinolin-5-yl)-3-(5-cyclopropyl-2-methylpyrazol-3 - yl)oxybenzonitrile
454		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(8-oxa-3 - azabicyclo[3.2.1]octan-3-yl)pyridin-4-yl]oxybenzonitrile
455		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(3-oxopiperazin-1-yl)pyridin-4-yl]oxybenzonitrile
456		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-methyl-6-(3-oxopiperazin-1-yl)pyridin-4-yl]oxybenzonitrile

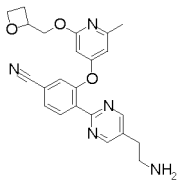
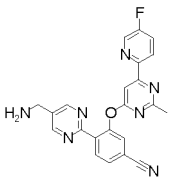
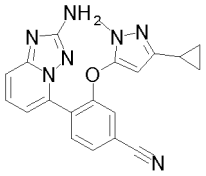
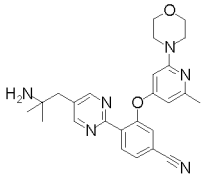
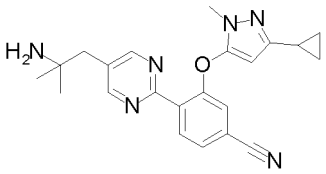
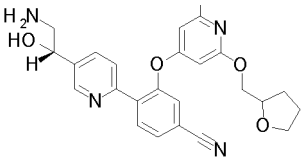
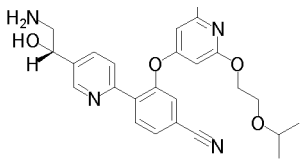
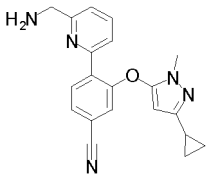
[Table 1-58]

Compound number	Structural formula	Compound name
457		4-[3 -(aminomethyl)-1,2-benzoxazol-6-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
458		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-[2-methoxyethyl(methyl)amino]-6-methylpyridin-4-yl] oxybenzonitrile
459		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-[2-methoxyethyl (methyl)amino]-6-methylpyridin-4-yl]oxybenzonitrile
460		2-amino-3-[1-[4-cyano-2-(5-ethyl-2-methylpyrazol-3-yl)oxyphenyl]indol-3-yl]propanoic acid
461		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(propan-2-ylamino)pyridin-4-yl]oxybenzonitrile
462		4-[5-(1-aminocyclopropyl)pyrimidin-2-yl] -3 -(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
463		4-[5-(1-aminocyclopropyl)pyrimidin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3 -yl)oxybenzonitrile
464		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-methyl-6-(4-methyl-3-oxopiperazin-1-yl)pyridin-4-yl] oxybenzonitrile

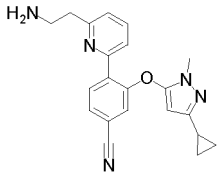
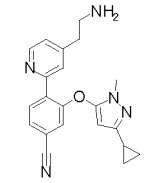
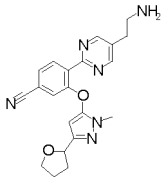
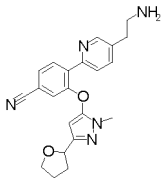
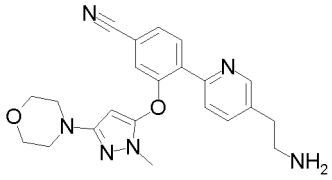
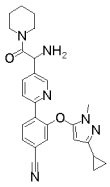
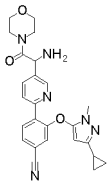
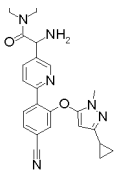
[Table 1-59]

Compound number	Structural formula	Compound name
465		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(4-methyl-3-oxopiperazin-1-yl)pyridin-4-yl] oxybenzonitrile
466		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(6-methylpyridazin-3 - yl)pyridin-4-yl]oxybenzonitrile
467		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
468		4-(5-aminopyrazolo[1,5-a]pyrimidin-7-yl)-3-(5-cyclopropyl-2-methylpyrazol-3 -yl)oxybenzonitrile
469		4-[5-(1-amino-2-hydroxyethyl)pyridin-2-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
470		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-[(3R)-3-methylmorpholin-4-yl]pyridin-4-yl] oxybenzonitrile
471		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-[(3 S)-3-methylmorpholin-4-yl]pyridin-4-yl] oxybenzonitrile
472		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-6-pyridin-2-ylpyrimidin-4-yl)oxybenzonitrile

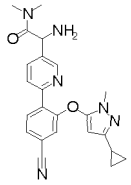
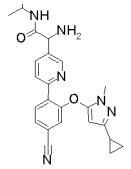
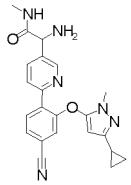
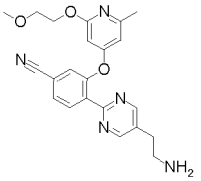
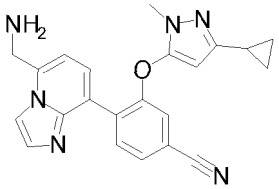
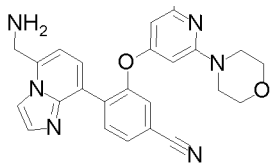
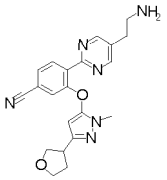
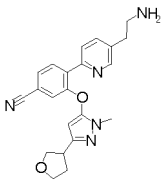
[Table 1-60]

Compound number	Structural formula	Compound name
473		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(oxetan-2-ylmethoxy)pyridin-4-yl]oxybenzonitrile
474		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(5-fluoropyridin-2-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile
475		4-(2-amino-[1,2,4]triazolo[1,5-a]pyridin-5-yl)-3-(5-cyclopropyl-2-methylpyrazol-3 -yl)oxybenzonitrile
476		4-[5-(2-amino-2-methylpropyl)pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
477		4-[5-(2-amino-2-methylpropyl)pyrimidin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3 - yl)oxybenzonitrile
478		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[2-methyl-6-(oxolan-2-ylmethoxy)pyridin-4-yl] oxybenzonitrile
479		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[2-methyl-6-(2-propan-2-yloxyethoxy)pyridin-4-yl] oxybenzonitrile
480		4-[6-(aminomethyl)pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3 - yl)oxybenzonitrile

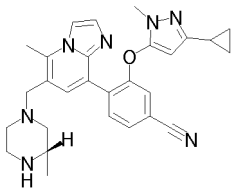
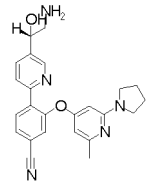
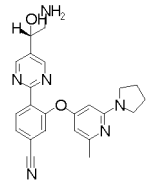
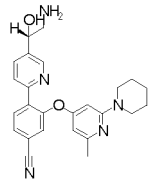
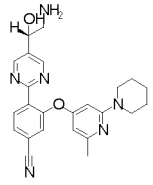
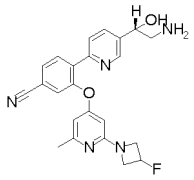
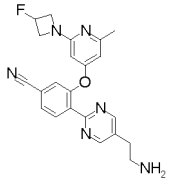
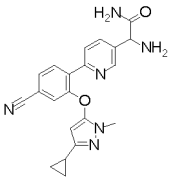
[Table 1-61]

Compound number	Structural formula	Compound name
481		4-[6-(2-aminoethyl)pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3 - yl)oxybenzonitrile
482		4-[4-(2-aminoethyl)pyridin-2-yl] -3 - (5-cyclopropyl-2-methylpyrazol-3 - yl)oxybenzonitrile
483		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-(oxolan-2-yl)pyrazol-3-yl]oxybenzonitrile
484		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-methyl-5-(oxolan-2-yl)pyrazol-3-yl]oxybenzonitrile
485		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-5-morpholin-4-ylpyrazol-3-yl)oxybenzonitrile
486		4-[5-(1-amino-2-oxo-2-piperidin-1-ylethyl)pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3 - yl)oxybenzonitrile
487		4-[5-(1-amino-2-morpholin-4-yl-2-oxoethyl)pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl) oxybenzonitrile
488		2-amino-2-[6-[4-cyano-2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxyphenyl]pyridin-3-yl]-N,N-diethylacetamide

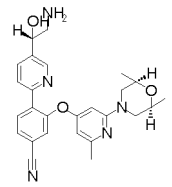
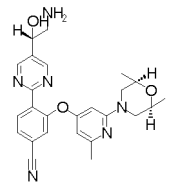
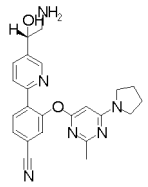
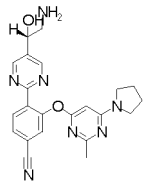
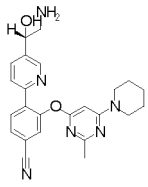
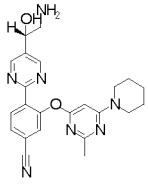
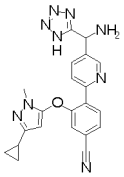
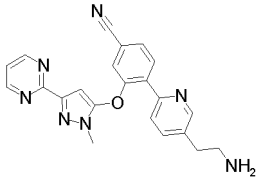
[Table 1-62]

Compound number	Structural formula	Compound name
489		2-amino-2-[6-[4-cyano-2-(5-cyclopropyl-2-methylpyrazol-3 -yl)oxyphenyl]pyridin-3-yl]-N,N-dimethylacetamide
490		2-amino-2-[6-[4-cyano-2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxyphenyl]pyridin-3-yl]-N-propan-2-ylacetamide
491		2-amino-2-[6-[4-cyano-2-(5-cyclopropyl-2-methylpyrazol-3 -yl)oxyphenyl]pyridin-3-yl]-N-methylacetamide
492		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-(2-methoxyethoxy)-6-methylpyridin-4-yl]oxybenzonitrile
493		4-[5-(aminomethyl)imidazo[1,2-a]pyridin-8-yl]-3-(5-cyclopropyl-2-methylpyrazol-3 -yl)oxybenzonitrile
494		4-[5-(aminomethyl)imidazo[1,2-a]pyridin-8-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
495		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-(oxolan-3-yl)pyrazol-3-yl]oxybenzonitrile
496		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-methyl-5-(oxolan-3-yl) pyrazol-3-yl]oxybenzonitrile

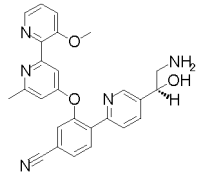
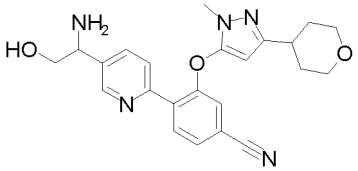
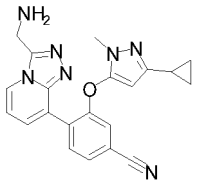
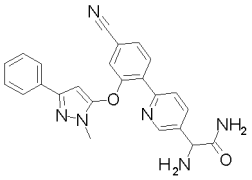
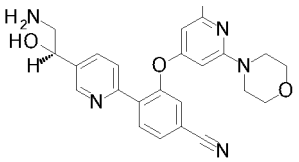
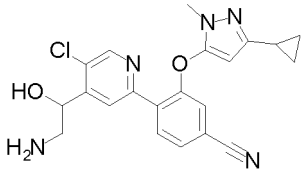
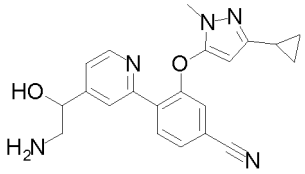
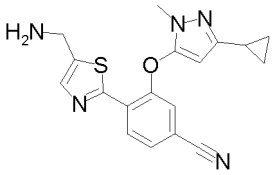
[Table 1-63]

Compound number	Structural formula	Compound name
497		3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxy-4-[5-methyl-6-[[(3S)-3-methylpiperazin-1-yl]methyl]imidazo[1,2-a]pyridin-8-yl]benzonitrile
498		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(2-methyl-6-pyrrolidin-1-ylpyridin-4-yl)oxybenzonitrile
499		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyrimidin-2-yl]-3-(2-methyl-6-pyrrolidin-1-ylpyridin-4-yl)oxybenzonitrile
500		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(2-methyl-6-piperidin-1-ylpyridin-4-yl)oxybenzonitrile
501		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyrimidin-2-yl]-3-(2-methyl-6-piperidin-1-ylpyridin-4-yl)oxybenzonitrile
502		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[2-(3-fluoroazetidin-1 -yl)-6-methylpyridin-4-yl]oxybenzonitrile
503		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-(3 -fluoroazetidin-1 -yl)-6-methylpyridin-4-yl]oxybenzonitrile
504		2-amino-2-[6-[4-cyano-2-(5-cyclopropyl-2-methylpyrazol-3-yl) oxyphenyl]pyridin-3-yl]acetamide

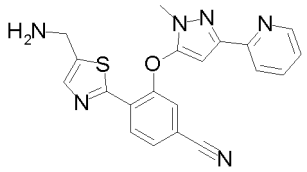
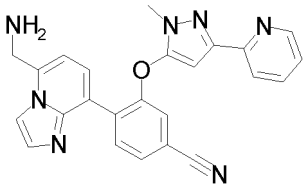
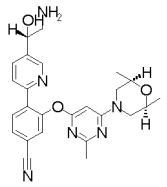
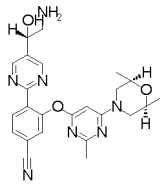
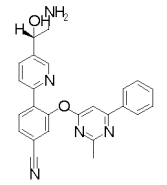
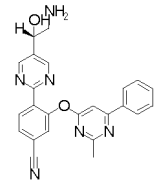
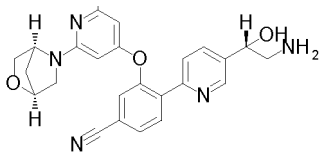
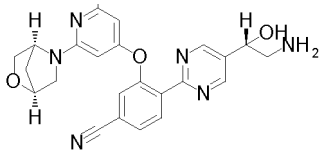
[Table 1-64]

Compound number	Structural formula	Compound name
505		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[2-[(2S,6R)-2,6-dimethylmorpholin-4-yl]-6-methylpyridin-4-yl] oxybenzonitrile
506		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyrimidin-2-yl]-3-[2-[(2S, 6R)-2,6-dimethylmorpholin-4-yl]-6-methylpyridin-4-yl] oxybenzonitrile
507		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(2-methyl-6-pyrrolidin-1 -ylpyrimidin-4-yl)oxybenzonitrile
508		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyrimidin-2-yl]-3-(2-methyl-6-pyrrolidin-1 -ylpyrimidin-4-yl)oxybenzonitrile
509		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(2-methyl-6-piperidin-1-ylpyrimidin-4-yl)oxybenzonitrile
510		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyrimidin-2-yl]-3-(2-methyl-6-piperidin-1-ylpyrimidin-4-yl)oxybenzonitrile
511		4-[5-[amino(1H-tetrazol-5-yl)methyl]pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3 - yl)oxybenzonitrile
512		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-5-pyrimidin-2-ylpyrazol-3-yl)oxybenzonitrile

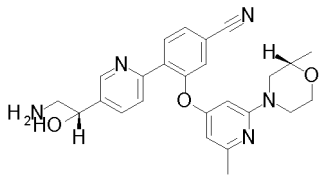
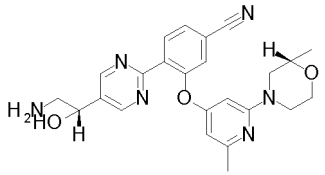
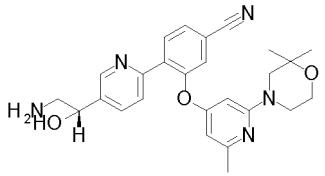
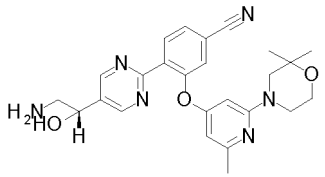
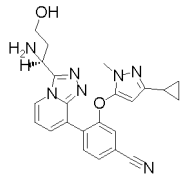
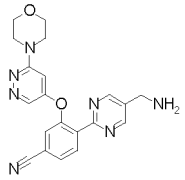
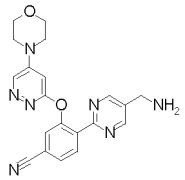
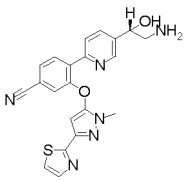
[Table 1-65]

Compound number	Structural formula	Compound name
513		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[2-(3-methoxypyridin-2-yl)-6-methylpyridin-4-yl]oxybenzonitrile
514		4-[5-(1-amino-2-hydroxyethyl)pyridin-2-yl]-3-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl]oxybenzonitrile
515		4-[3 -(aminomethyl)-[1,2,4]triazolo[4,3-a]pyridin-8-yl]-3-(5-cyclopropyl-2-methylpyrazol-3- yl)oxybenzonitrile
516		2-amino-2-[6-[4-cyano-2-(2-methyl-5-phenylpyrazol-3-yl) oxyphenyl]pyridin-3-yl]acetamide
517		4-[5-[(1R)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
518		4-[4-(2-amino-1-hydroxyethyl)-5-chloropyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3 -yl)oxybenzonitrile
519		4-[4-(2-amino-1-hydroxyethyl)pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3- yl)oxybenzonitrile
520		4-[5-(aminomethyl)-1,3-thiazol-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile

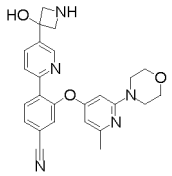
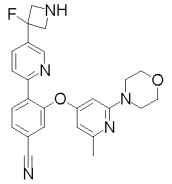
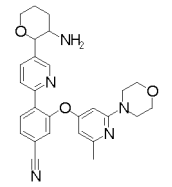
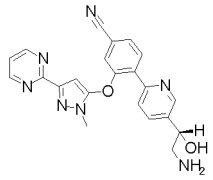
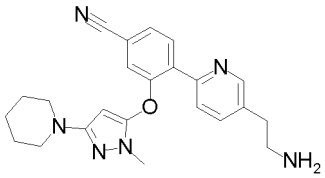
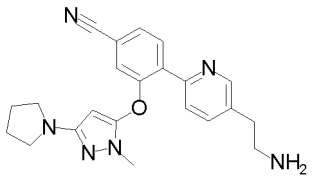
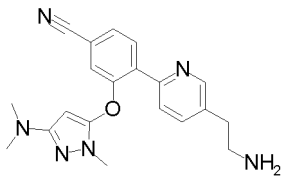
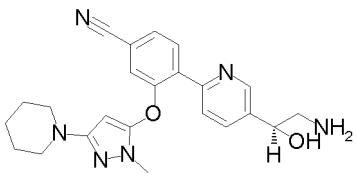
[Table 1-66]

Compound number	Structural formula	Compound name
521		4-[5-(aminomethyl)-1,3-thiazol-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
522		4-[5-(aminomethyl)imidazo[1,2-a]pyridin-8-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
523		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[6-[(2S,6R)-2,6-dimethylmorpholin-4-yl]-2-methylpyrimidin-4-yl] oxybenzonitrile
524		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyrimidin-2-yl]-3-[6-[(2S,6R)-2,6-dimethylmorpholin-4-yl]-2-methylpyrimidin-4-yl] oxybenzonitrile
525		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile
526		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyrimidin-2-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile
527		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[2-methyl-6-[(1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl]pyridin-4-yl] oxybenzonitrile
528		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyrimidin-2-yl]-3-[2-methyl-6-[(1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl]pyridin-4-yl] oxybenzonitrile

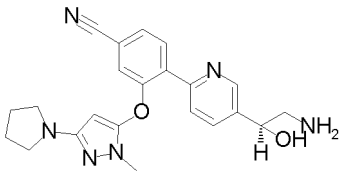
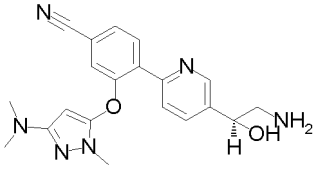
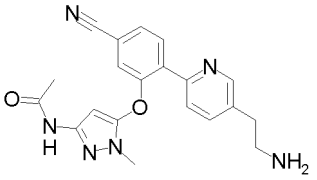
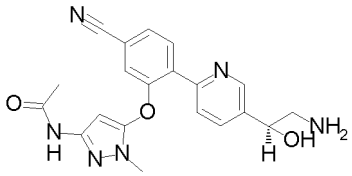
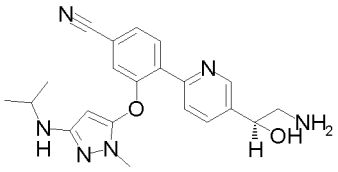
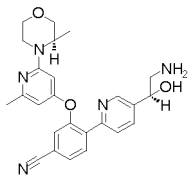
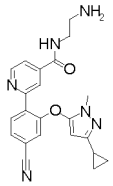
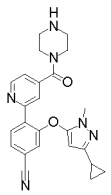
[Table 1-67]

Compound number	Structural formula	Compound name
529		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[2-methyl-6-[(2S)-2-methylmorpholin-4-yl]pyridin-4-yl]oxybenzonitrile
530		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyrimidin-2-yl]-3-[2-methyl-6-[(2S)-2-methylmorpholin-4-yl]pyridin-4-yl] oxybenzonitrile
531		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[2-(2,2-dimethylmorpholin-4-yl)-6-methylpyridin-4-yl] oxybenzonitrile
532		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyrimidin-2-yl]-3-[2-(2,2-dimethylmorpholin-4-yl)-6-methylpyridin-4-yl] oxybenzonitrile
533		4-[3-(1-amino-3-hydroxypropyl)-[1,2,4]triazolo[4,3-a]pyridin-8-yl]-3-(5-cyclopropyl-2-methylpyrazol-3- yl)oxybenzonitrile
534		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(6-morpholin-4-ylpyridazin-4-yl)oxybenzonitrile
535		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(5-morpholin-4-ylpyridazin-3-yl)oxybenzonitrile
536		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[2-methyl-5-(1,3-thiazol-2-yl)pyrazol-3-yl]oxybenzonitrile

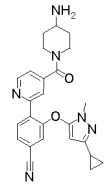
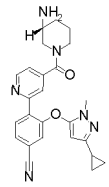
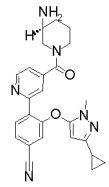
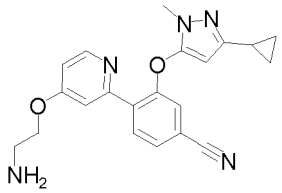
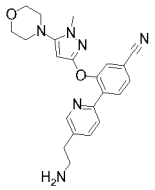
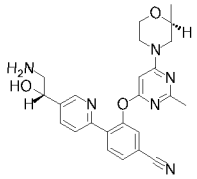
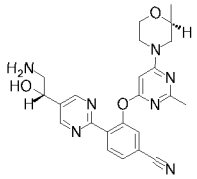
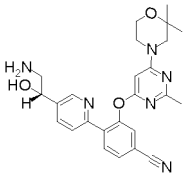
[Table 1-68]

Compound number	Structural formula	Compound name
537		4-[5-(3-hydroxyazetidin-3-yl)pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
538		4-[5-(3-fluoroazetidin-3-yl)pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
539		4-[5-(3-aminooxan-2-yl)pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
540		4-[5-[(1 S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(2-methyl-5-pyrimidin-2-ylpyrazol-3-yl)oxybenzonitrile
541		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-5-piperidin-1-ylpyrazol-3-yl)oxybenzonitrile
542		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-5-pyrrolidin-1-ylpyrazol-3- yl)oxybenzonitrile
543		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[5-(dimethylamino)-2-methylpyrazol-3-yl]oxybenzonitrile
544		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(2-methyl-5-piperidin-1-ylpyrazol-3-yl)oxybenzonitrile

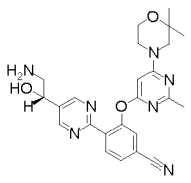
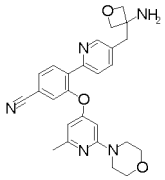
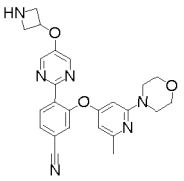
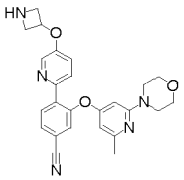
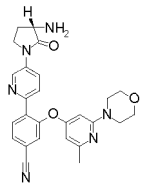
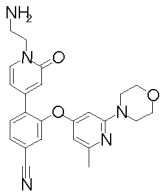
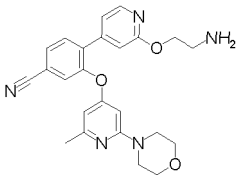
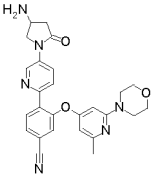
[Table 1-69]

Compound number	Structural formula	Compound name
545		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(2-methyl-5-pyrrolidin-1-ylpyrazol-3- yl)oxybenzonitrile
546		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[5-(dimethylamino)-2-methylpyrazol-3-yl] oxybenzonitrile
547		N-[5-[2-[5-(2-aminoethyl)pyridin-2-yl]-5-cyanophenoxy]-1-methylpyrazol-3 -yl]acetamide
548		N-[5-[2-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-5-cyanophenoxy]-1-methylpyrazol-3-yl]acetamide
549		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[2-methyl-5-(propan-2-ylamino)pyrazol-3-yl]oxybenzonitrile
550		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[2-methyl-6-[(3R)-3-methylmorpholin-4-yl]pyridin-4-yl] oxybenzonitrile
551		N-(2-aminoethyl)-2-[4-cyano-2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxyphenyl]pyridine-4-carboxamide
552		3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxy-4-[4-(piperazine-1-carbonyl)pyridin-2-yl]benzonitrile

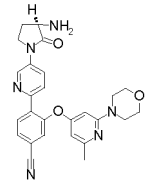
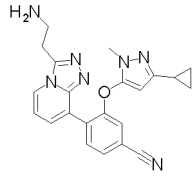
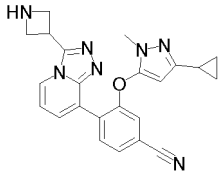
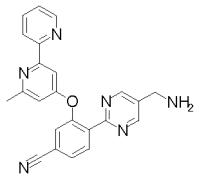
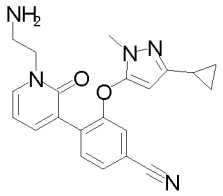
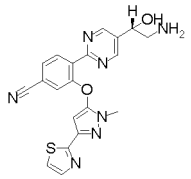
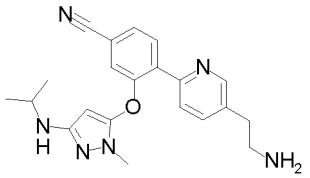
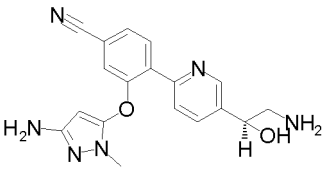
[Table 1-70]

Compound number	Structural formula	Compound name
553		4-[4-(4-aminopiperidine-1-carbonyl)pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
554		4-[4-[(3R)-3-aminopiperidine-1-carbonyl]pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
555		4-[4-[(3S)-3-aminopiperidine-1- carbonyl]pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
556		4-[4-(2-aminoethoxy)pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
557		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(1-methyl-5-morpholin-4-ylpyrazol-3-yl)oxybenzonitrile
558		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[2-methyl-6-[(2S)-2-methylmorpholin-4-yl]pyrimidin-4-yl]oxybenzonitrile
559		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyrimidin-2-yl]-3-[2-methyl-6-[(2S)-2-methylmorpholin-4-yl]pyrimidin-4-yl] oxybenzonitrile
560		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[6-(2,2-dimethylmorpholin-4-yl)-2-methylpyrimidin-4-yl] oxybenzonitrile

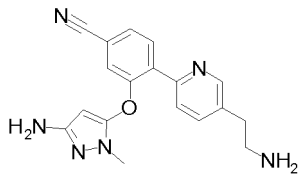
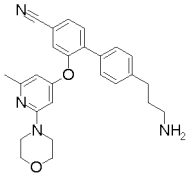
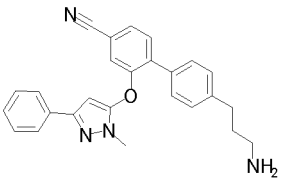
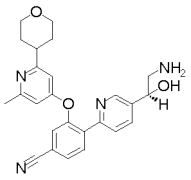
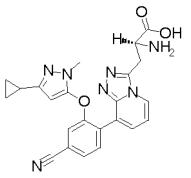
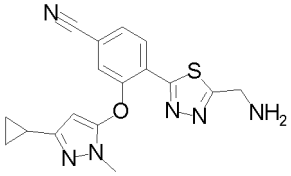
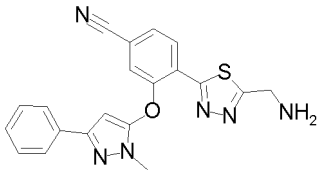
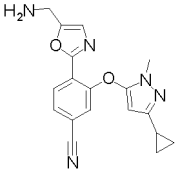
[Table 1-71]

Compound number	Structural formula	Compound name
561		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyrimidin-2-yl]-3-[6-(2,2-dimethylmorpholin-4-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile
562		4-[5-[(3-aminooxetan-3- yl)methyl]pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
563		4-[5-(azetidin-3-yloxy)pyrimidin-2-yl]-3 -(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
564		4-[5-(azetidin-3-yloxy)pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
565		4-[5-[(3S)-3-amino-2-oxopyrrolidin-1-yl]pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
566		4-[1-(2-aminoethyl)-2-oxopyridin-4-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
567		4-[2-(2-aminoethoxy)pyridin-4-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
568		4-[5-(4-amino-2-oxopyrrolidin-1-yl)pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile

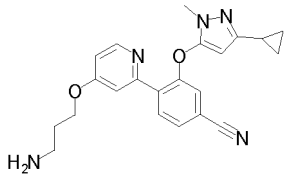
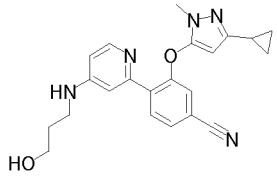
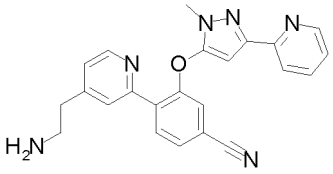
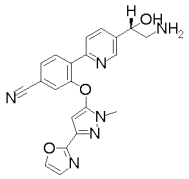
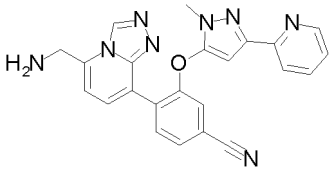
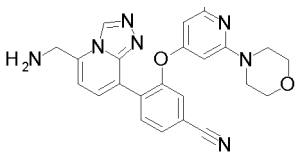
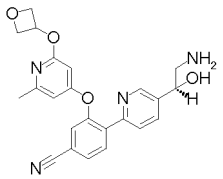
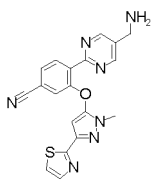
[Table 1-72]

Compound number	Structural formula	Compound name
569		4-[5-[(3R)-3-amino-2-oxopyrrolidin-1-yl]pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl) oxybenzonitrile
570		4-[3-(2-aminoethyl)-[1,2,4]triazolo[4,3-a]pyridin-8-yl]-3-(5-cyclopropyl-2-methylpyrazol-3 - yl)oxybenzonitrile
571		4-[3 -(azetidin-3-yl)-[1,2,4]triazolo[4,3-a]pyridin-8-yl]-3-(5-cyclopropyl-2-methylpyrazol-3- yl))oxybenzonitrile
572		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-6-pyridin-2-ylpyridin-4-yl)oxybenzonitrile
573		4-[1-(2-aminoethyl)-2-oxopyridin-3-yl]-3-(5-cyclopropyl-2-methylpyrazol-3 -yl)oxybenzonitrile
574		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyrimidin-2-yl]-3-[2-methyl-5-(1,3-thiazol-2-yl)pyrazol-3-yl]oxybenzonitrile
575		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-methyl-5-(propan-2-ylamino)pyrazol-3-yl]oxybenzonitrile
576		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(5-amino-2-methylpyrazol-3-yl)oxybenzonitrile

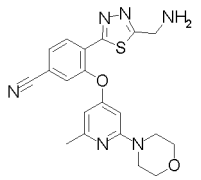
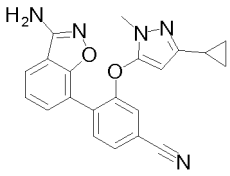
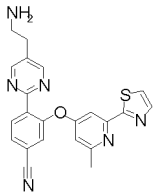
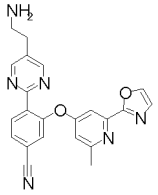
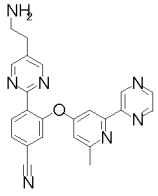
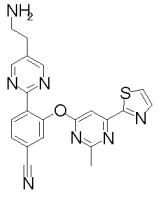
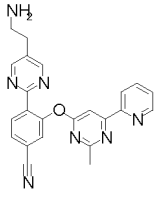
[Table 1-73]

Compound number	Structural formula	Compound name
577		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(5-amino-2-methylpyrazol-3- yl)oxybenzonitrile
578		4-[4-(3-aminopropyl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
579		4-[4-(3-aminopropyl)phenyl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
580		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[2-methyl-6-(oxan-4-yl)pyridin-4-yl]oxybenzonitrile
581		2-amino-3-[8-[4-cyano-2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxyphenyl]-[1,2,4]triazolo[4,3-a]pyridin-3-yl]propanoic acid
582		4-[5-(aminomethyl)-1,3,4-thiadiazol-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3 -yl)oxybenzonitrile
583		4-[5-(aminomethyl)-1,3,4-thiadiazol-2-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
584		4-[5-(aminomethyl)-1,3-oxazol-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile

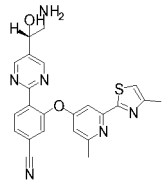
[Table 1-74]

Compound number	Structural formula	Compound name
585		4-[4-(3-aminopropoxy)pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
586		3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxy-4-[4-(3-hydroxypropylamino)pyridin-2-yl]benzonitrile
587		4-[4-(2-aminoethyl)pyridin-2-yl] -3 - (2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
588		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[2-methyl-5-(1,3-oxazol-2-yl)pyrazol-3-yl]oxybenzonitrile
589		4-[5-(aminomethyl)-[1,2,4]triazolo[4,3-a]pyridin-8-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
590		4-[5-(aminomethyl)-[1,2,4]triazolo[4,3-a]pyridin-8-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
591		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[2-methyl-6-(oxetan-3-yloxy)pyridin-4-yl]oxybenzonitrile
592		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5 -(1,3 -thiazol-2-yl)pyrazol-3-yl]oxybenzonitrile

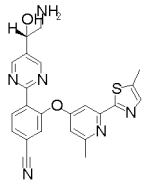
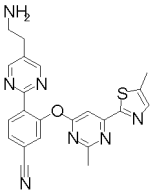
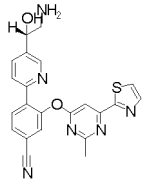
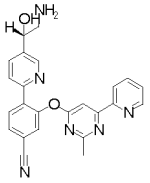
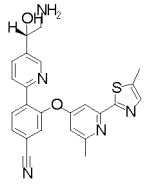
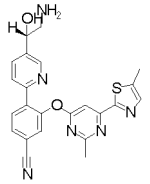
[Table 1-75]

Compound number	Structural formula	Compound name
593		4-[5-(aminomethyl)-1,3,4-thiazol-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
594		4-(3 -amino-1,2-benzoxazol-7-yl)-3- (5-cyclopropyl-2-methylpyrazol-3- yl)oxybenzonitrile
595		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(1,3 -thiazol-2-yl)pyridin-4-yl]oxybenzonitrile
596		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(1,3-oxazol-2-yl)pyridin-4-yl]oxybenzonitrile
597		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-pyrazin-2-ylpyridin-4-yl)oxybenzonitrile
598		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(1,3 -thiazol-2-yl)pyrimidin-4-yl]oxybenzonitrile
599		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-pyridin-2-ylpyrimidin-4-yl)oxybenzonitrile

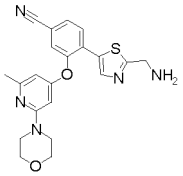
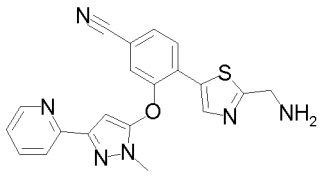
(continued)

Compound number	Structural formula	Compound name
600		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyrimidin-2-yl]-3-[2-methyl-6-(4-methyl-1,3-thiazol-2-yl)pyridin-4-yl]oxybenzonitrile

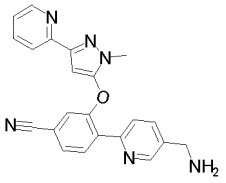
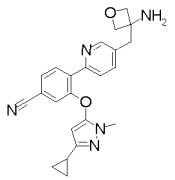
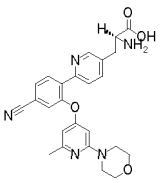
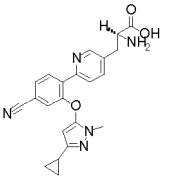
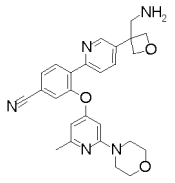
[Table 1-76]

Compound number	Structural formula	Compound name
601		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyrimidin-2-yl]-3-[2-methyl-6-(5-methyl-1,3-thiazol-2-yl)pyridin-4-yl] oxybenzonitrile
602		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(5-methyl-1,3-thiazol-2-yl)pyrimidin-4-yl]oxybenzonitrile
603		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[2-methyl-6-(1,3-thiazol-2-yl)pyrimidin-4-yl]oxybenzonitrile
604		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(2-methyl-6-pyridin-2-ylpyrimidin-4-yl)oxybenzonitrile
605		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[2-methyl-6-(5-methyl-1,3-thiazol-2-yl)pyridin-4-yl] oxybenzonitrile
606		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[2-methyl-6-(5-methyl-1,3-thiazol-2-yl)pyrimidin-4-yl] oxybenzonitrile

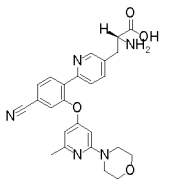
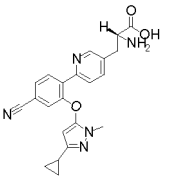
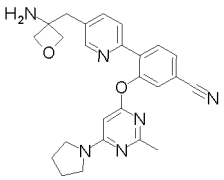
(continued)

Compound number	Structural formula	Compound name
607		4-[2-(aminomethyl)-1,3-thiazol-5-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
608		4-[2-(aminomethyl)-1,3-thiazol-5-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile

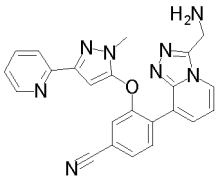
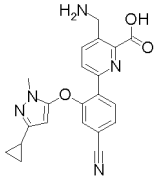
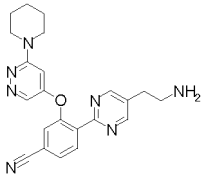
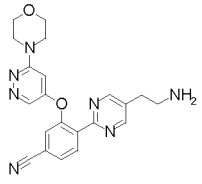
[Table 1-77]

Compound number	Structural formula	Compound name
609		4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
610		4-[5-[(3 -aminooxetan-3- yl)methyl]pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
611		(2S)-2-amino-3-[6-[4-cyano-2-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxyphenyl]pyridin-3-yl]propanoic acid
612		(2S)-2-amino-3-[6-[4-cyano-2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxyphenyl]pyridin-3-yl]propanoic acid
613		4-[5-[3 -(aminomethyl)oxetan-3- yl]pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile

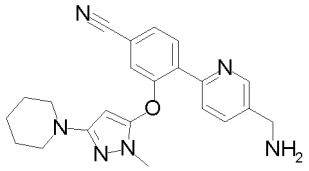
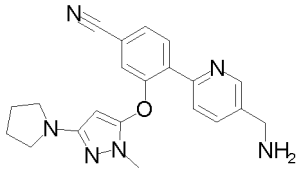
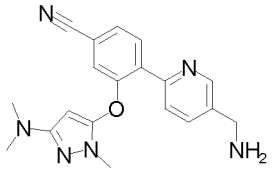
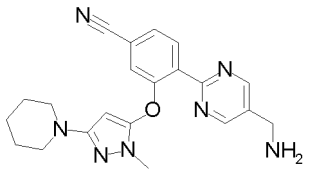
(continued)

Compound number	Structural formula	Compound name
614		(2R)-2-amino-3-[6-[4-cyano-2-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxyphenyl]pyridin-3-yl]propanoic acid
615		(2R)-2-amino-3-[6-[4-cyano-2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxyphenyl]pyridin-3-yl]propanoic acid
616		4-[5-[(3-aminooxetan-3- yl)methyl]pyridin-2-yl]-3-(2-methyl-6-pyrrolidin-1-ylpyrimidin-4-yl)oxybenzonitrile

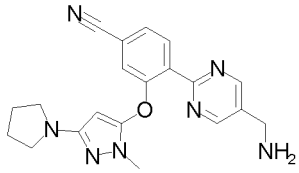
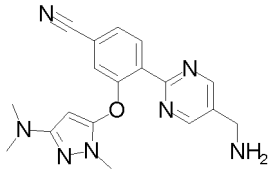
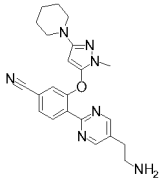
[Table 1-78]

Compound number	Structural formula	Compound name
617		4-[3-(aminomethyl)-[1,2,4]triazolo[4,3-a]pyridin-8-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
618		3-(aminomethyl)-6-[4-cyano-2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxyphenyl]pyridine-2-carboxylic acid
619		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(6-piperidin-1 -ylpyridazin-4-yl)oxybenzonitrile
620		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(6-morpholin-4-ylpyridazin-4-yl)oxybenzonitrile

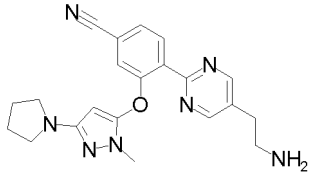
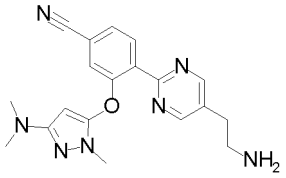
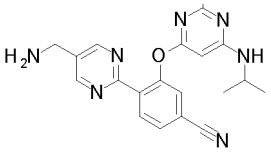
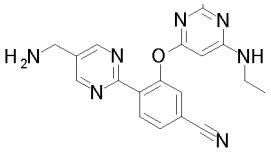
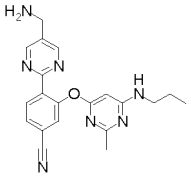
(continued)

Compound number	Structural formula	Compound name
621		4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-5-piperidin-1-ylpyrazol-3-yl)oxybenzonitrile
622		4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-5 -pyrrolidin-1 -ylpyrazol-3- yl)oxybenzonitrile
623		4-[5-(aminomethyl)pyridin-2-yl]-3-[5-(dimethylamino)-2-methylpyrazol-3-yl]oxybenzonitrile
624		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-piperidin-1-ylpyrazol-3-yl)oxybenzonitrile

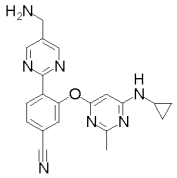
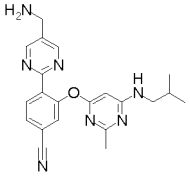
[Table 1-79]

Compound number	Structural formula	Compound name
625		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5 -pyrrolidin-1-ylpyrazol-3 - yl)oxybenzonitrile
626		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-(dimethylamino)-2-methylpyrazol-3-yl]oxybenzonitrile
627		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-piperidin-1-ylpyrazol-3-yl)oxybenzonitrile

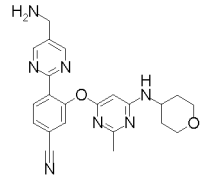
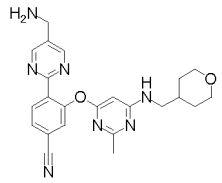
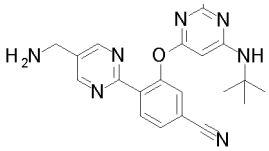
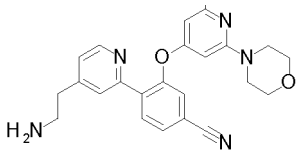
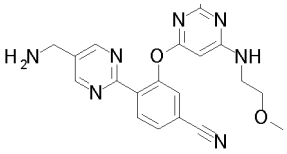
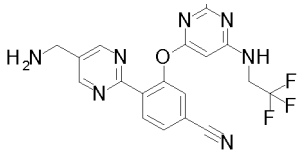
(continued)

Compound number	Structural formula	Compound name
628		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5 -pyrrolidin-1-ylpyrazol-3 - yl)oxybenzonitrile
629		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-(dimethylamino)-2-methylpyrazol-3-yl]oxybenzonitrile
630		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-6-(propan-2-ylamino)pyrimidin-4-yl]oxybenzonitrile
631		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(ethylamino)-2-methylpyrimidin-4-yl]oxybenzonitrile
632		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-6-(propylamino) pyrimidin-4-yl]oxybenzonitrile

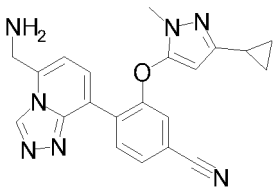
[Table 1-80]

Compound number	Structural formula	Compound name
633		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(cyclopropylamino)-2-methylpyrimidin-4-yl]oxybenzonitrile
634		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-6-(2-methylpropylamino)pyrimidin-4-yl]oxybenzonitrile

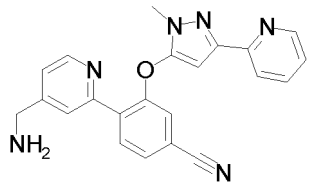
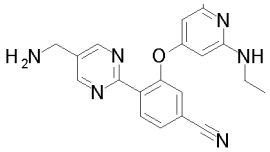
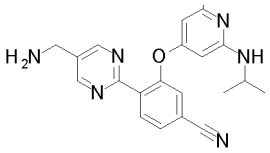
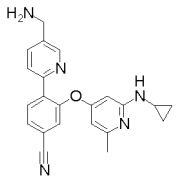
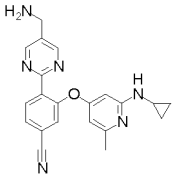
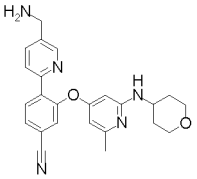
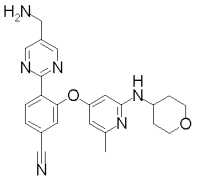
(continued)

Compound number	Structural formula	Compound name
635		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-6-(oxan-4-ylamino)pyrimidin-4-yl]oxybenzonitrile
636		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-6-(oxan-4-ylmethylamino)pyrimidin-4-yl]oxybenzonitrile
637		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(tert-butylamino)-2-methylpyrimidin-4-yl]oxybenzonitrile
638		4-[4-(2-aminoethyl)pyridin-2-yl]-3 - (2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
639		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(2-methoxyethylamino)-2-methylpyrimidin-4-yl]oxybenzonitrile
640		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-6-(2,2,2-trifluoroethylamino)pyrimidin-4-yl]oxybenzonitrile

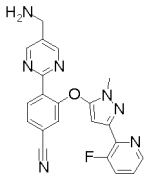
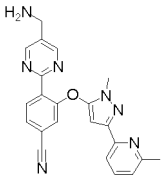
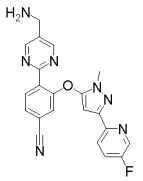
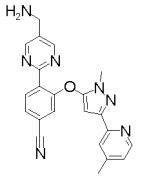
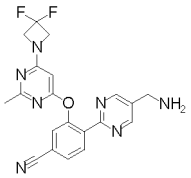
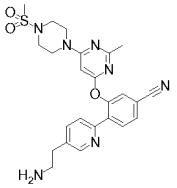
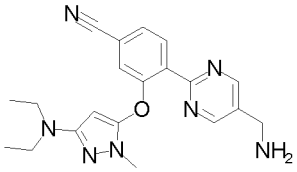
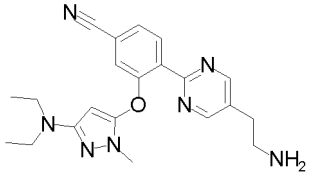
[Table 1-81]

Compound number	Structural formula	Compound name
641		4-[5-(aminomethyl)-[1,2,4]triazolo[4,3-a]pyridin-8-yl]-3-(5-cyclopropyl-2-methylpyrazol-3 - yl)oxybenzonitrile

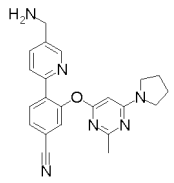
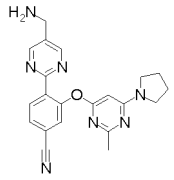
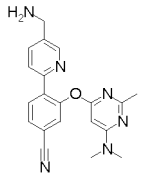
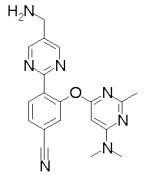
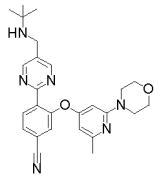
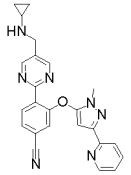
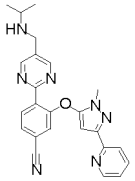
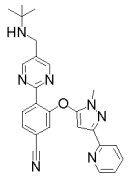
(continued)

Compound number	Structural formula	Compound name
642		4-[4-(aminomethyl)pyridin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
643		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-(ethylamino)-6-methylpyridin-4-yl]oxybenzonitrile
644		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-6-(propan-2-ylamino)pyridin-4-yl]oxybenzonitrile
645		4-[5-(aminomethyl)pyridin-2-yl]-3-[2-(cyclopropylamino)-6-methylpyridin-4-yl]oxybenzonitrile
646		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-(cyclopropylamino)-6-methylpyridin-4-yl]oxybenzonitrile
647		4-[5-(aminomethyl)pyridin-2-yl]-3-[2-methyl-6-(oxan-4-ylamino) pyridin-4-yl]oxybenzonitrile
648		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-6-(oxan-4-ylamino) pyridin-4-yl]oxybenzonitrile

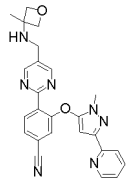
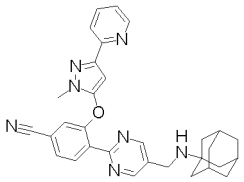
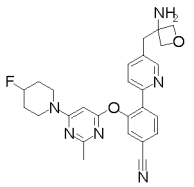
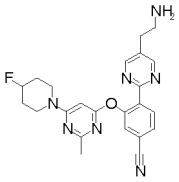
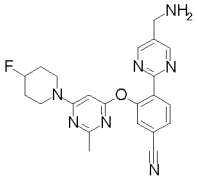
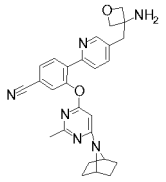
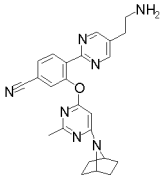
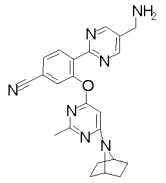
[Table 1-82]

Compound number	Structural formula	Compound name
649		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-(3-fluoropyridin-2-yl)-2-methylpyrazol-3 -yl]oxybenzonitrile
650		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(6-methylpyridin-2-yl)pyrazol-3 -yl]oxybenzonitrile
651		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-(5-fluoropyridin-2-yl)-2-methylpyrazol-3 -yl]oxybenzonitrile
652		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(4-methylpyridin-2-yl)pyrazol-3 -yl]oxybenzonitrile
653		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(3,3-difluoroazetidin-1-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile
654		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-methyl-6-(4-methylsulfonylpiperazin-1-yl)pyrimidin-4-yl]oxybenzonitrile
655		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-(diethylamino)-2-methylpyrazol-3-yl]oxybenzonitrile
656		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-(diethylamino)-2-methylpyrazol-3-yl]oxybenzonitrile

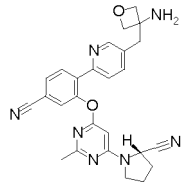
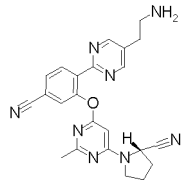
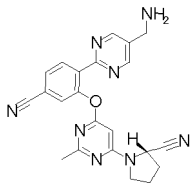
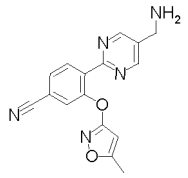
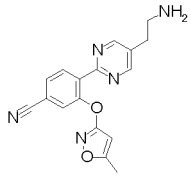
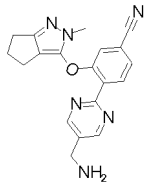
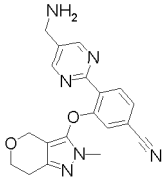
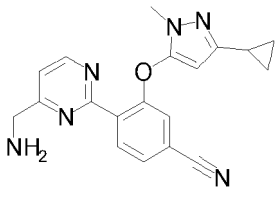
[Table 1-83]

Compound number	Structural formula	Compound name
657		4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-6-pyrrolidin-1-ylpyrimidin-4-yl) oxybenzonitrile
658		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-6-pyrrolidin-1-ylpyrimidin-4-yl)oxybenzonitrile
659		4-[5-(aminomethyl)pyridin-2-yl]-3-[6-(dimethylamino)-2-methylpyrimidin-4-yl]oxybenzonitrile
660		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(dimethylamino)-2-methylpyrimidin-4-yl]oxybenzonitrile
661		4-[5-[(tert-butylamino)methyl]pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
662		4-[5-[(cyclopropylamino)methyl]pyrimidin -2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3 -yl)oxybenzonitrile
663		3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxy-4-[5-[(propan-2-ylamino)methyl] pyrimidin-2-yl]benzonitrile
664		4-[5-[(tert-butylamino)methyl]pyrimidin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile

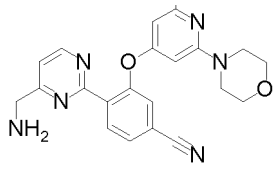
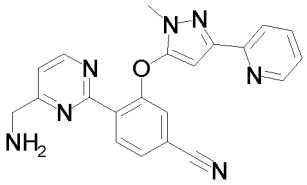
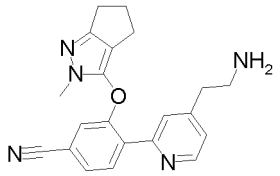
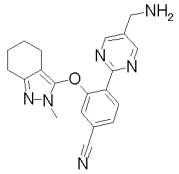
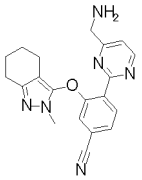
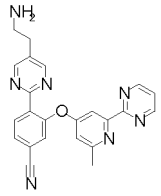
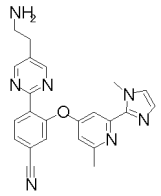
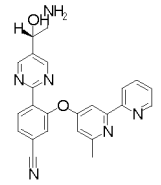
[Table 1-84]

Compound number	Structural formula	Compound name
665		4-[5-[[(3-methyloxetan-3-yl)amino]methyl]pyrimidin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
666		4-[5-[(1-adamantylamino)methyl]pyrimidin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
667		4-[5-[(3-aminooxetan-3-yl)methyl]pyridin-2-yl]-3-[6-(4-fluoropiperidin-1-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile
668		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[6-(4-fluoropiperidin-1-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile
669		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(4-fluoropiperidin-1-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile
670		4-[5-[(3-aminooxetan-3-yl)methyl]pyridin-2-yl]-3-[6-(7-azabicyclo[2.2.1]heptan-7-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile
671		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[6-(7-azabicyclo[2.2.1]heptan-7-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile
672		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(7-azabicyclo[2.2.1]heptan-7-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile

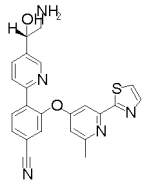
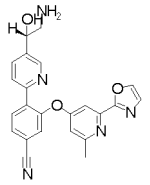
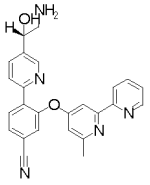
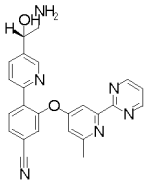
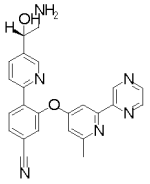
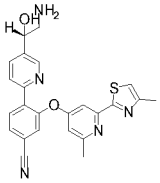
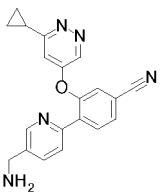
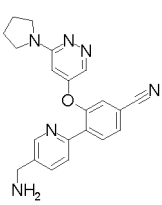
[Table 1-85]

Compound number	Structural formula	Compound name
673		(2S)-1-[6-[2-[5-[(3-aminooxetan-3-yl)methyl]pyridin-2-yl]-5-cyanophenoxy]-2-methylpyrimidin-4-yl]pyrrolidine-2-carbonitrile
674		(2S)-1-[6-[2-[5-(2-aminoethyl)pyrimidin-2-yl]-5-cyanophenoxy]-2-methylpyrimidin-4-yl]pyrrolidine-2-carbonitrile
675		(2S)-1-[6-[2-[5-(aminomethyl)pyrimidin-2-yl]-5-cyanophenoxy]-2-methylpyrimidin-4-yl]pyrrolidine-2-carbonitrile
676		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[(5-methyl-1,2-oxazol-3-yl) oxy]benzonitrile
677		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(5-methyl-1,2-oxazol-3-yl) oxy]benzonitrile
678		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[(2-methyl-5,6-dihydro-4H-cyclopenta[c]pyrazol-3-yl)oxy]benzonitrile
679		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[(2-methyl-6,7-dihydro-4H-pyrano[4,3-c]pyrazol-3-yl)oxy]benzonitrile
680		4-[4-(aminomethyl)pyrimidin-2-yl]-3 - (5-cyclopropyl-2-methylpyrazol-3- yl)oxybenzonitrile

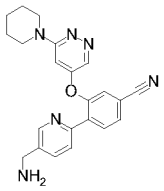
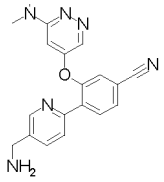
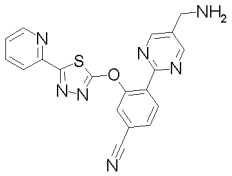
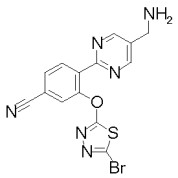
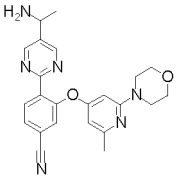
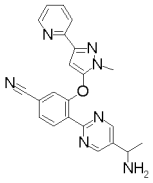
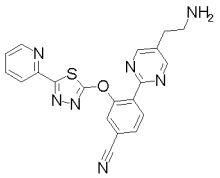
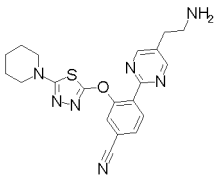
[Table 1-86]

Compound number	Structural formula	Compound name
681		4-[4-(aminomethyl)pyrimidin-2-yl]-3 - (2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
682		4-[4-(aminomethyl)pyrimidin-2-yl]-3 - (2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
683		4-[4-(2-aminoethyl)pyridin-2-yl] -3 - [(2-methyl-5,6-dihydro-4H-cyclopenta[c]pyrazol-3-yl)oxy]benzonitrile
684		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[(2-methyl-4,5,6,7-tetrahydroindazol-3-yl)oxy]benzonitrile
685		4-[4-(aminomethyl)pyrimidin-2-yl]-3 - [(2-methyl-4,5,6,7-tetrahydroindazol-3-yl)oxy]benzonitrile
686		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-pyrimidin-2-ylpyridin-4-yl)oxybenzonitrile
687		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(1-methylimidazol-2-yl)pyridin-4-yl]oxybenzonitrile
688		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyrimidin-2-yl]-3-(2-methyl-6-pyridin-2-ylpyridin-4-yl)oxybenzonitrile

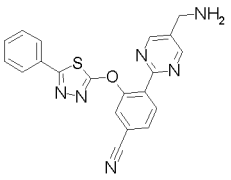
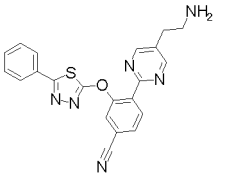
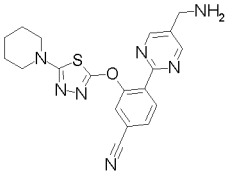
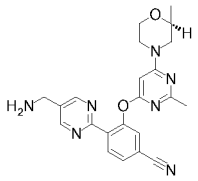
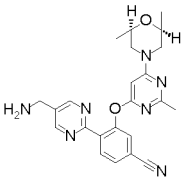
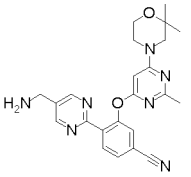
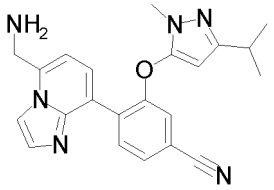
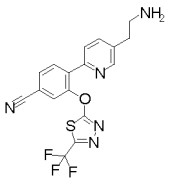
[Table 1-87]

Compound number	Structural formula	Compound name
689		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[2-methyl-6-(1,3-thiazol-2-yl)pyridin-4-yl]oxybenzonitrile
690		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[2-methyl-6-(1,3-oxazol-2-yl)pyridin-4-yl]oxybenzonitrile
691		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(2-methyl-6-pyridin-2-ylpyridin-4-yl)oxybenzonitrile
692		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(2-methyl-6-pyrimidin-2-ylpyridin-4-yl)oxybenzonitrile
693		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-(2-methyl-6-pyrazin-2-ylpyridin-4-yl)oxybenzonitrile
694		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[2-methyl-6-(4-methyl-1,3-thiazol-2-yl)pyridin-4-yl]oxybenzonitrile
695		4-[5-(aminomethyl)pyridin-2-yl]-3-(6-cyclopropylpyridazin-4-yl) oxybenzonitrile
696		4-[5-(aminomethyl)pyridin-2-yl]-3-(6-pyrrolidin-1-ylpyridazin-4-yl) oxybenzonitrile

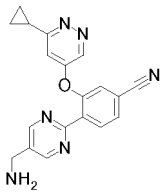
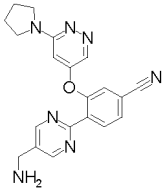
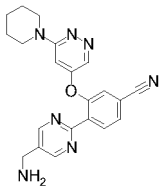
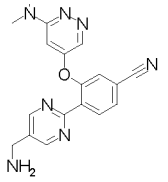
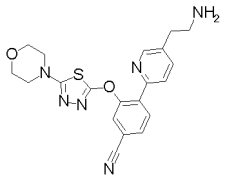
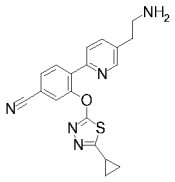
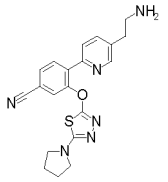
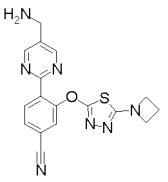
[Table 1-88]

Compound number	Structural formula	Compound name
697		4-[5-(aminomethyl)pyridin-2-yl]-3-(6-piperidin-1-ylpyridazin-4-yl) oxybenzonitrile
698		4-[5-(aminomethyl)pyridin-2-yl]-3-[6-(dimethylamino)pyridazin-4-yl]oxybenzonitrile
699		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[(5-pyridin-2-yl-1,3,4-thiadiazol-2-yl)oxy]benzonitrile
700		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[(5-bromo-1,3,4-thiadiazol-2-yl)oxy]benzonitrile
701		4-[5-(1-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
702		4-[5-(1-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
703		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(5-pyridin-2-yl-1,3,4-thiadiazol-2-yl)oxy]benzonitrile
704		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(5-piperidin-1-yl-1,3,4-thiadiazol-2-yl)oxy]benzonitrile

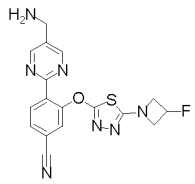
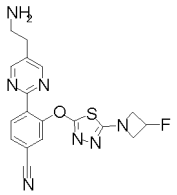
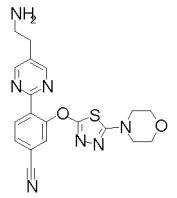
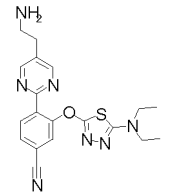
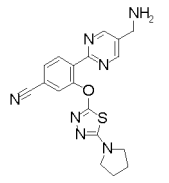
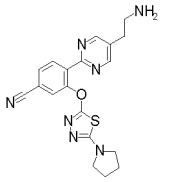
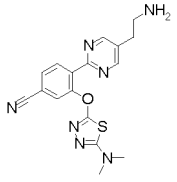
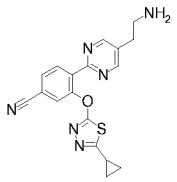
[Table 1-89]

Compound number	Structural formula	Compound name
705		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[(5-phenyl-1,3,4-thiadiazol-2-yl)oxy]benzonitrile
706		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(5-phenyl-1,3,4-thiadiazol-2-yl)oxy]benzonitrile
707		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[(5-piperidin-1-yl-1,3,4-thiadiazol-2-yl)oxy]benzonitrile
708		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-6-[(2S)-2-methylmorpholin-4-yl]pyrimidin-4-yl]oxybenzonitrile
709		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-2-methylpyrimidin-4-yl] oxybenzonitrile
710		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(2,2-dimethylmorpholin-4-yl)-2-methylpyrimidin-4-yl] oxybenzonitrile
711		4-[5-(aminomethyl)imidazo[1,2-a]pyridin-8-yl]-3-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxybenzonitrile
712		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]oxy]benzonitrile

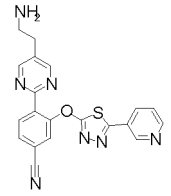
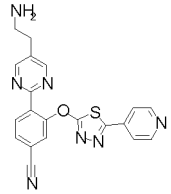
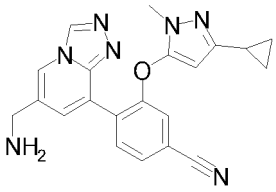
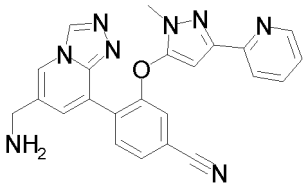
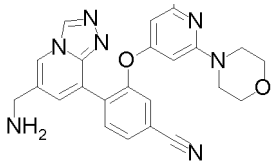
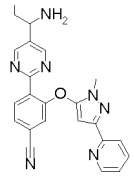
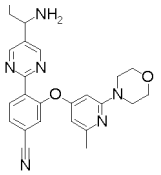
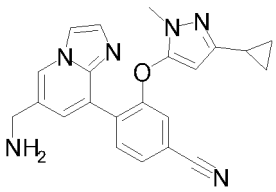
[Table 1-90]

Compound number	Structural formula	Compound name
713		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(6-cyclopropylpyridazin-4-yl) oxybenzonitrile
714		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(6-pyrrolidin-1-ylpyridazin-4-yl) oxybenzonitrile
715		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(6-piperidin-1-ylpyridazin-4-yl) oxybenzonitrile
716		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(dimethylamino)pyridazin-4-yl] oxybenzonitrile
717		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[(5-morpholin-4-yl-1,3,4-thiadiazol-2-yl) oxy]benzonitrile
718		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[(5-cyclopropyl-1,3,4-thiadiazol-2-yl)oxy] benzonitrile
719		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[(5-pyrrolidin-1-yl-1,3,4-thiadiazol-2-yl) oxy]benzonitrile
720		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[[5-(azetidin-1-yl)-1,3,4-thiadiazol-2-yl] oxy]benzonitrile

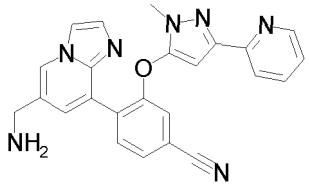
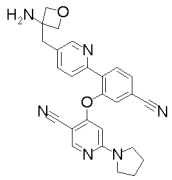
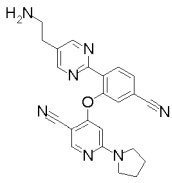
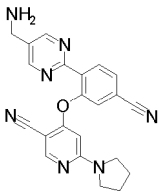
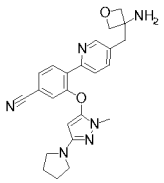
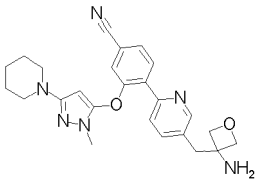
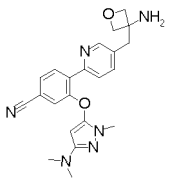
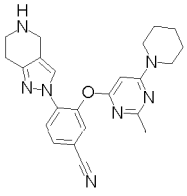
[Table 1-91]

Compound number	Structural formula	Compound name
721		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[[5-(3-fluoroazetidin-1-yl)-1,3,4-thiadiazol-2-yl]oxy]benzonitrile
722		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[[5-(3-fluoroazetidin-1-yl)-1,3,4-thiadiazol-2-yl]oxy]benzonitrile
723		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(5-morpholin-4-yl-1,3,4-thiadiazol-2-yl)oxy]benzonitrile
724		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[[5-(diethylamino)-1,3,4-thiadiazol-2-yl]oxy]benzonitrile
725		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[(5-pyrrolidin-1-yl-1,3,4-thiadiazol-2-yl)oxy]benzonitrile
726		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(5-pyrrolidin-1-yl-1,3,4-thiadiazol-2-yl)oxy]benzonitrile
727		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[[5-(dimethylamino)-1,3,4-thiadiazol-2-yl]oxy]benzonitrile
728		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(5-cyclopropyl-1,3,4-thiadiazol-2-yl)oxy]benzonitrile

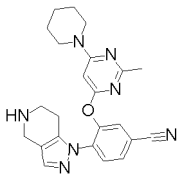
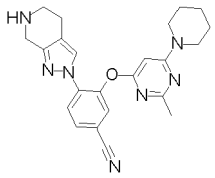
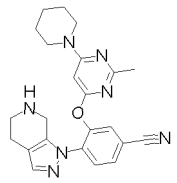
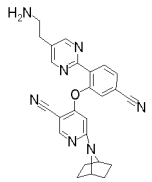
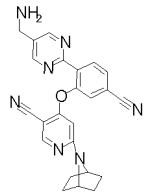
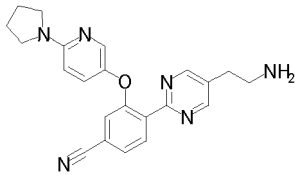
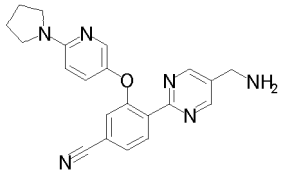
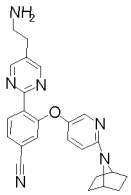
[Table 1-92]

Compound number	Structural formula	Compound name
729		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(5-pyridin-3-yl-1,3,4-thiadiazol-2-yl)oxy]benzonitrile
730		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(5-pyridin-4-yl-1,3,4-thiadiazol-2-yl)oxy]benzonitrile
731		4-[6-(aminomethyl)-[1,2,4]triazolo[4,3-a]pyridin-8-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
732		4-[6-(aminomethyl)-[1,2,4]triazolo[4,3-a]pyridin-8-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
733		4-[6-(aminomethyl)-[1,2,4]triazolo[4,3-a]pyridin-8-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
734		4-[5-(1-aminopropyl)pyrimidin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
735		4-[5-(1-aminopropyl)pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
736		4-[6-(aminomethyl)imidazo[1,2-a]pyridin-8-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile

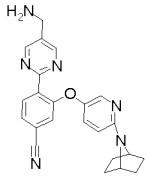
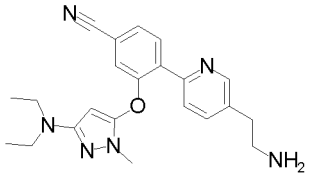
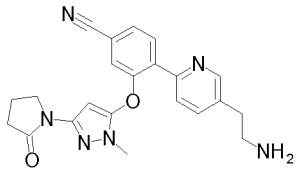
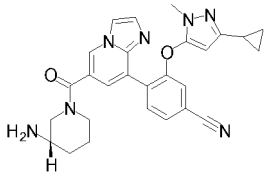
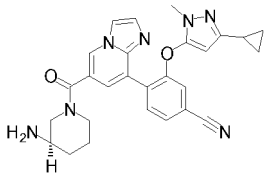
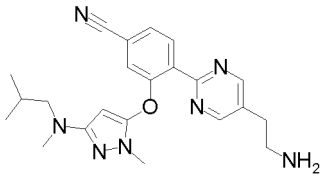
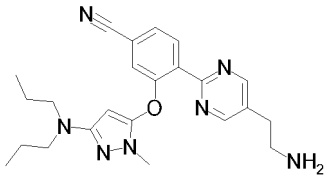
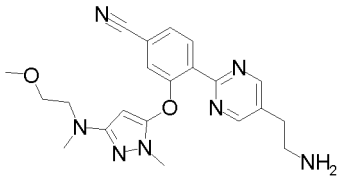
[Table 1-93]

Compound number	Structural formula	Compound name
737		4-[6-(aminomethyl)imidazo[1,2-a]pyridin-8-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
738		4-[2-[5-[(3 -aminooxetan-3 - yl)methyl]pyridin-2-yl]-5-cyanophenoxy]-6-pyrrolidin-1-ylpyridine-3-carbonitrile
739		4-[2-[5-(2-aminoethyl)pyrimidin-2-yl]-5-cyanophenoxy]-6-pyrrolidin-1-ylpyridine-3-carbonitrile
740		4-[2-[5-(aminomethyl)pyrimidin-2-yl]-5-cyanophenoxy]-6-pyrrolidin-1- ylpyridine-3-carbonitrile
741		4-[5-[(3-aminooxetan-3- yl)methyl]pyridin-2-yl]-3-(2-methyl-5-pyrrolidin-1-ylpyrazol-3-yl)oxybenzonitrile
742		4-[5-[(3-aminooxetan-3- yl)methyl]pyridin-2-yl]-3-(2-methyl-5-piperidin-1-ylpyrazol-3-yl)oxybenzonitrile
743		4-[5-[(3-aminooxetan-3- yl)methyl]pyridin-2-yl]-3-[5-(dimethylamino)-2-methylpyrazol-3- yl]oxybenzonitrile
744		3-(2-methyl-6-piperidin-1-ylpyrimidin-4-yl)oxy-4-(4,5,6,7-tetrahydropyrazolo[4,3-c]pyridin-2-yl)benzonitrile

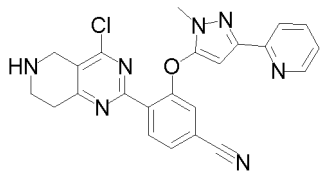
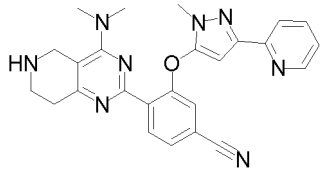
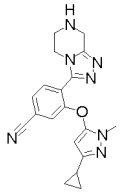
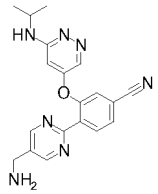
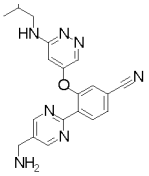
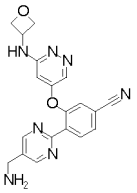
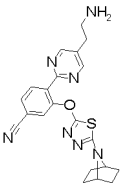
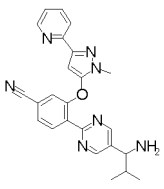
[Table 1-94]

Compound number	Structural formula	Compound name
745		3-(2-methyl-6-piperidin-1-ylpyrimidin-4-yl)oxy-4-(4,5,6,7-tetrahydropyrazolo[4,3-c]pyridin-1-yl)benzonitrile
746		3-(2-methyl-6-piperidin-1-ylpyrimidin-4-yl)oxy-4-(4,5,6,7-tetrahydropyrazolo[3,4-c]pyridin-2-yl)benzonitrile
747		3-(2-methyl-6-piperidin-1-ylpyrimidin-4-yl)oxy-4-(4,5,6,7-tetrahydropyrazolo[3,4-c]pyridin-1-yl)benzonitrile
748		4-[2-[5-(2-aminoethyl)pyrimidin-2-yl]-5-cyanophenoxy]-6-(7-azabicyclo[2.2. 1]heptan-7-yl)pyridine-3-carbonitrile
749		4-[2-[5-(aminomethyl)pyrimidin-2-yl]-5-cyanophenoxy]-6-(7-azabicyclo[2.2. 1]heptan-7-yl)pyridine-3-carbonitrile
750		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(6-pyrrolidin-1-ylpyridin-3-yl)oxybenzonitrile
751		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(6-pyrrolidin-1-ylpyridin-3-yl)oxybenzonitrile
752		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[6-(7-azabicyclo[2.2.1]heptan-7-yl)pyridin-3-yl]oxybenzonitrile

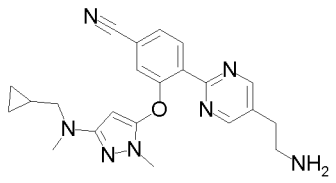
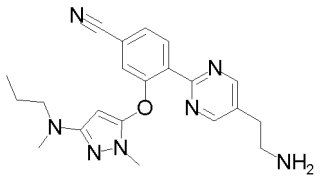
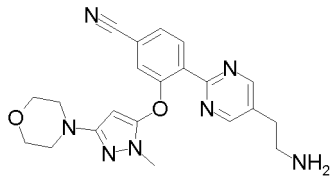
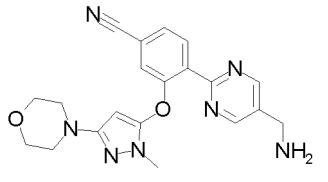
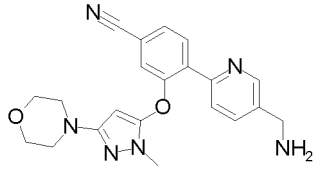
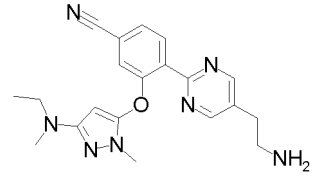
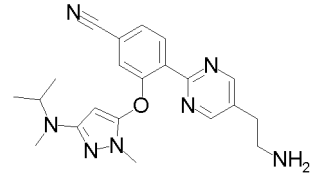
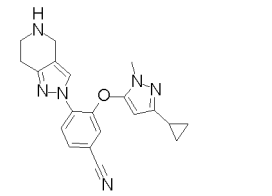
[Table 1-95]

Compound number	Structural formula	Compound name
753		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(7-azabicyclo[2.2.1] heptan-7-yl)pyridin-3-yl]oxybenzonitrile
754		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[5-(diethylamino)-2-methylpyrazol-3-yl]oxybenzonitrile
755		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-methyl-5-(2-oxopyrrolidin-1-yl)pyrazol-3 -yl]oxybenzonitrile
756		4-[6-[(3S)-3-aminopiperidine-1-carbonyl]imidazo[1,2-a] pyridin-8-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl) oxybenzonitrile
757		4-[6-[(3R)-3-aminopiperidine-1-carbonyl]imidazo[1,2-a] pyridin-8-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl) oxybenzonitrile
758		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-[methyl(2-methylpropyl)amino]pyrazol-3-yl]oxybenzonitrile
759		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-(dipropylamino)-2-methylpyrazol-3-yl]oxybenzonitrile
760		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-[2-methoxyethyl (methyl)amino]-2-methylpyrazol-3 -yl]oxybenzonitrile

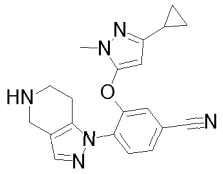
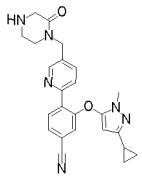
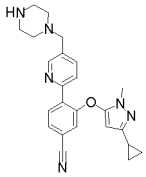
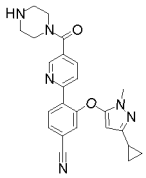
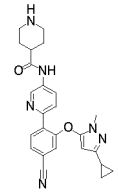
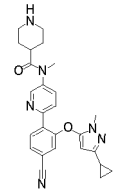
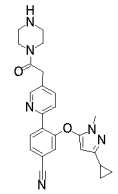
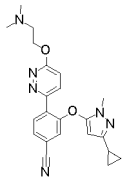
[Table 1-96]

Compound number	Structural formula	Compound name
761		4-(4-chloro-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-2-yl)-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl))oxybenzonitrile
762		4-[4-(dimethylamino)-5,6,7,8-tetrahydropyrido[4,3-d] pyrimidin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl) oxybenzonitrile
763		3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxy-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3- yl)benzonitrile
764		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(propan-2-ylamino) pyridazin-4-yl]oxybenzonitrile
765		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(2-methylpropylamino)pyridazin-4-yl]oxybenzonitrile
766		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(oxetan-3-ylamino) pyridazin-4-yl]oxybenzonitrile
767		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[[5-(7-azabicyclo[2.2.1] heptan-7-yl)-1,3,4-thiadiazol-2-yl]oxy]benzonitrile
768		4-[5-(1-amino-2-methylpropyl)pyrimidin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile

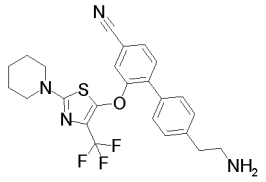
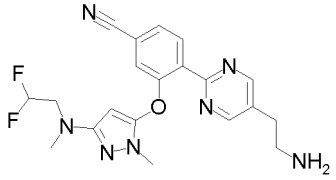
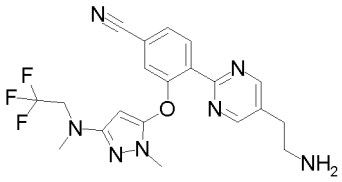
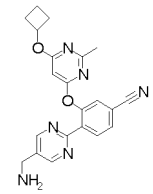
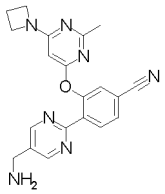
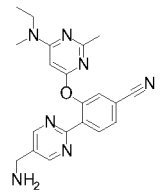
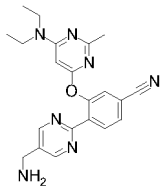
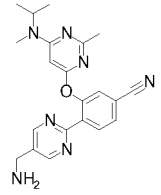
[Table 1-97]

Compound number	Structural formula	Compound name
769		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-[cyclopropylmethyl (methyl)amino]-2-methylpyrazol-3 -yl]oxybenzonitrile
770		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-[methyl (propyl)amino]pyrazol-3- yl]oxybenzonitrile
771		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-morpholin-4-ylpyrazol-3-yl)oxybenzonitrile
772		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-morpholin-4-ylpyrazol-3-yl)oxybenzonitrile
773		4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-5-morpholin-4-ylpyrazol-3-yl)oxybenzonitrile
774		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-[ethyl(methyl)amino]-2-methylpyrazol-3-yl]oxybenzonitrile
775		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-[methyl (propan-2-yl)amino]pyrazol-3-yl]oxybenzonitrile
776		3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxy-4-(4,5,6,7-tetrahydropyrazolo[4,3-c]pyridin-2-yl)benzonitrile

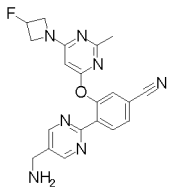
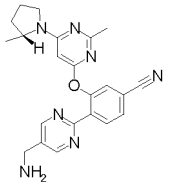
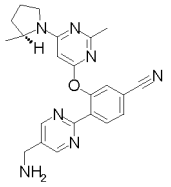
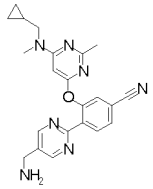
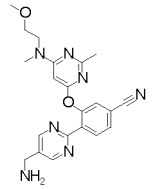
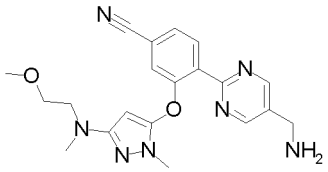
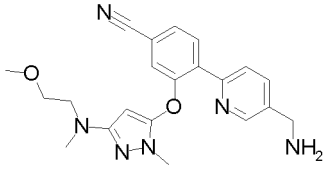
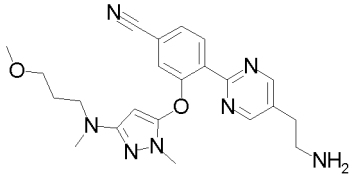
[Table 1-98]

Compound number	Structural formula	Compound name
777		3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxy-4-(4,5,6,7-tetrahydropyrazolo[4,3-c]pyridin-1-yl)benzonitrile
778		3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxy-4-[5-[(2-oxopiperazin-1- yl)methyl]pyridin-2-yl]benzonitrile
779		3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxy-4-[5-(piperazin-1-ylmethyl)pyridin-2-yl]benzonitrile
780		3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxy-4-[5-(piperazine-1-carbonyl)pyridin-2-yl]benzonitrile
781		N-[6-[4-cyano-2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxyphenyl] pyridin-3-yl]piperidine-4-carboxamide
782		N-[6-[4-cyano-2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxyphenyl] pyridin-3-yl]-N-methylpiperidine-4-carboxamide
783		3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxy-4-[5-(2-oxo-2-piperazin-1-ylethyl)pyridin-2-yl]benzonitrile
784		3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxy-4-[6-[2-(dimethylamino) ethoxy]pyridazin-3- yl]benzonitrile

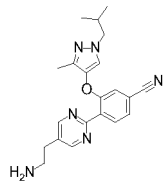
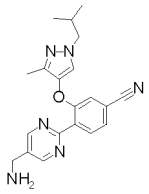
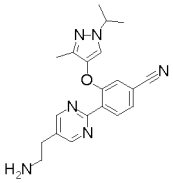
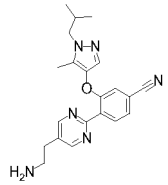
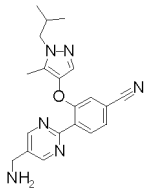
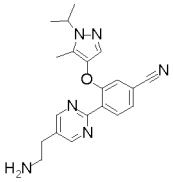
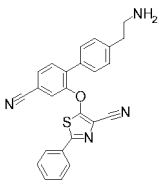
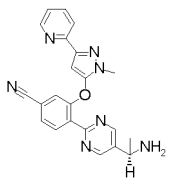
[Table 1-99]

Compound number	Structural formula	Compound name
785		4-[4-(2-aminoethyl)phenyl]-3-[[2-piperidin-1-yl-4-(trifluoromethyl)-1,3-thiazol-5-yl]oxy]benzonitrile
786		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-[2,2-difluoroethyl(methyl)amino]-2-methylpyrazol-3-yl]oxybenzonitrile
787		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-[methyl(2,2,2-trifluoroethyl)amino]pyrazol-3-yl]oxybenzonitrile
788		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(6-cyclobutyloxy-2-methylpyrimidin-4-yl)oxybenzonitrile
789		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(azetidin-1-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile
790		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-[ethyl(methyl)amino]-2-methylpyrimidin-4-yl]oxybenzonitrile
791		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(diethylamino)-2-methylpyrimidin-4-yl]oxybenzonitrile
792		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-6-[methyl(propan-2-yl)amino]pyrimidin-4-yl]oxybenzonitrile

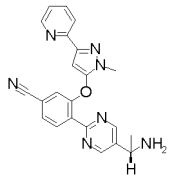
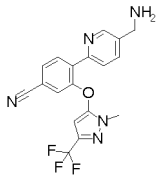
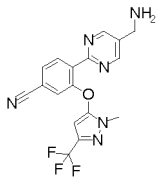
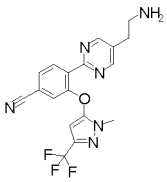
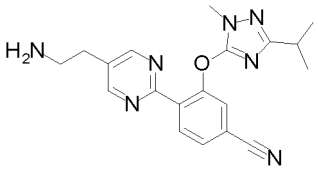
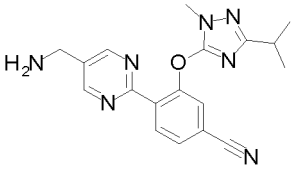
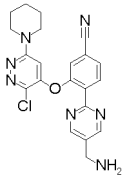
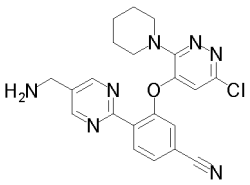
[Table 1-100]

Compound number	Structural formula	Compound name
793		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(3-fluoroazetidin-1-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile
794		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-6-[(2R)-2-methylpyrrolidin-1-yl]pyrimidin-4-yl]oxybenzonitrile
795		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-6-[(2S)-2-methylpyrrolidin-1-yl]pyrimidin-4-yl]oxybenzonitrile
796		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-[cyclopropylmethyl(methyl)amino]-2-methylpyrimidin-4-yl]oxybenzonitrile
797		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-[2-methoxyethyl(methyl)amino]-2-methylpyrimidin-4-yl]oxybenzonitrile
798		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-[2-methoxyethyl(methyl)amino]-2-methylpyrazol-3 -yl]oxybenzonitrile
799		4-[5-(aminomethyl)pyridin-2-yl]-3-[5-[2-methoxyethyl(methyl)amino]-2-methylpyrazol-3-yl]oxybenzonitrile
800		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-[3-methoxypropyl(methyl)amino]-2-methylpyrazol-3-yl]oxybenzonitrile

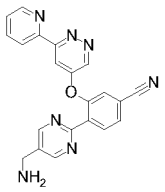
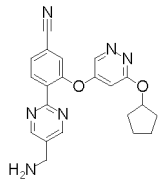
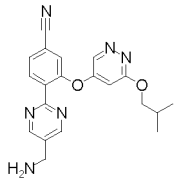
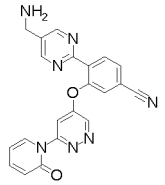
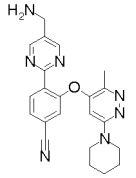
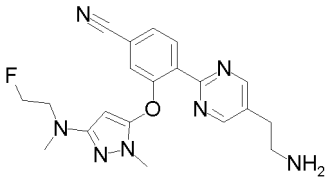
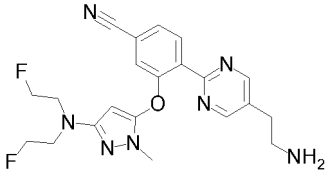
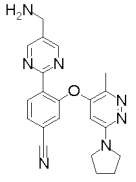
[Table 1-101]

Compound number	Structural formula	Compound name
801		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[3-methyl-1-(2-methylpropyl) pyrazol-4-yl]oxybenzonitrile
802		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[3-methyl-1-(2-methylpropyl) pyrazol-4-yl]oxybenzonitrile
803		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(3-methyl-1-propan-2-ylpyrazol-4-yl)oxybenzonitrile
804		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-methyl-1-(2-methylpropyl) pyrazol-4-yl]oxybenzonitrile
805		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-methyl-1-(2-methylpropyl) pyrazol-4-yl]oxybenzonitrile
806		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-methyl-1-propan-2-ylpyrazol-4-yl)oxybenzonitrile
807		5-[2-[4-(2-aminoethyl)phenyl]-5-cyanophenoxy]-2-phenyl-1,3-thiazole-4-carbonitrile
808		4-[5-[(1R)-1-aminoethyl]pyrimidin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile

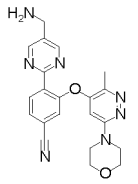
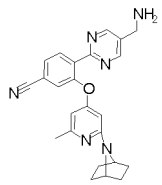
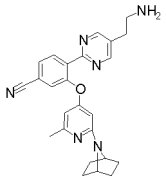
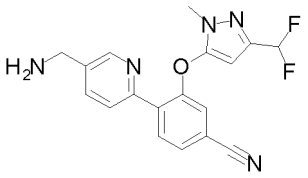
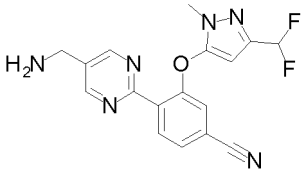
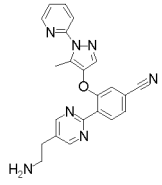
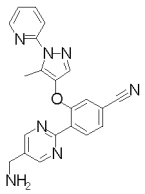
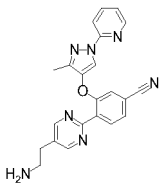
[Table 1-102]

Compound number	Structural formula	Compound name
809		4-[5-[(1S)-1-aminoethyl]pyrimidin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
810		4-[5-(aminomethyl)pyridin-2-yl]-3-[2-methyl-5-(trifluoromethyl)pyrazol-3-yl]oxybenzonitrile
811		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(trifluoromethyl)pyrazol-3-yl]oxybenzonitrile
812		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-(trifluoromethyl)pyrazol-3-yl]oxybenzonitrile
813		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(2-methyl-5-propan-2-yl-1,2,4-triazol-3-yl)oxy]benzonitrile
814		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[(2-methyl-5-propan-2-yl-1,2,4-triazol-3-yl)oxy]benzonitrile
815		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(3-chloro-6-piperidin-1-ylpyridazin-4-yl)oxybenzonitrile
816		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(6-chloro-3-piperidin-1-ylpyridazin-4-yl)oxybenzonitrile

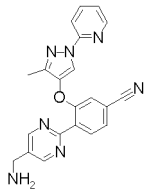
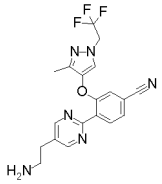
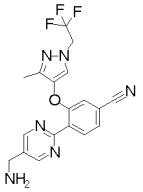
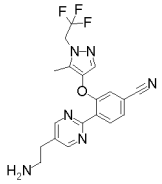
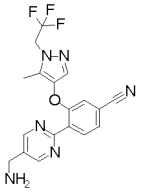
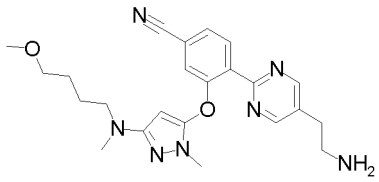
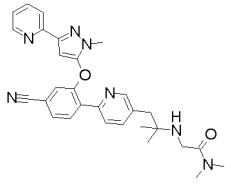
[Table 1-103]

Compound number	Structural formula	Compound name
817		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(6-pyridin-2-ylpyridazin-4-yl) oxybenzonitrile
818		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(6-cyclopentyloxypyridazin-4-yl)oxybenzonitrile
819		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(2-methylpropoxy) pyridazin-4-yl]oxybenzonitrile
820		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(2-oxopyridin-1-yl) pyridazin-4-yl]oxybenzonitrile
821		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(3-methyl-6-piperidin-1-ylpyridazin-4-yl)oxybenzonitrile
822		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-[2-fluoroethyl(methyl) amino]-2-methylpyrazol-3-yl]oxybenzonitrile
823		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-[bis(2-fluoroethyl)amino]-2-methylpyrazol-3 -yl]oxybenzonitrile
824		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(3-methyl-6-pyrrolidin-1-ylpyridazin-4-yl)oxybenzonitrile

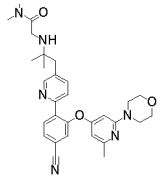
[Table 1-104]

Compound number	Structural formula	Compound name
825		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(3-methyl-6-morpholin-4-ylpyridazin-4-yl)oxybenzonitrile
826		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-(7-azabicyclo[2.2.1]heptan-7-yl)-6-methylpyridin-4-yl]oxybenzonitrile
827		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-(7-azabicyclo[2.2.1]heptan-7-yl)-6-methylpyridin-4-yl]oxybenzonitrile
828		4-[5-(aminomethyl)pyridin-2-yl]-3-[5-(difluoromethyl)-2-methylpyrazol-3-yl]oxybenzonitrile
829		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-(difluoromethyl)-2-methylpyrazol-3-yl]oxybenzonitrile
830		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-methyl-1-pyridin-2-ylpyrazol-4-yl)oxybenzonitrile
831		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(5-methyl-1-pyridin-2-ylpyrazol-4-yl)oxybenzonitrile
832		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(3-methyl-1-pyridin-2-ylpyrazol-4-yl)oxybenzonitrile

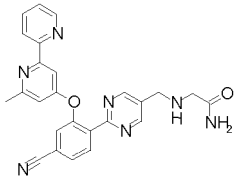
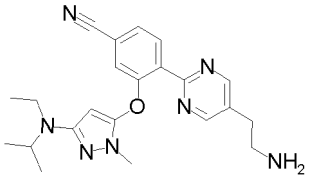
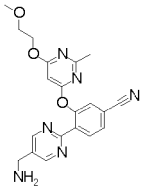
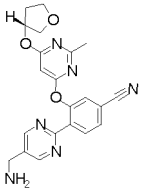
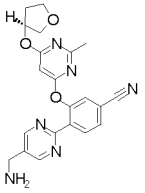
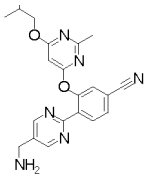
[Table 1-105]

Compound number	Structural formula	Compound name
833		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(3-methyl-1-pyridin-2-ylpyrazol-4-yl)oxybenzonitrile
834		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[3-methyl-1-(2,2,2-trifluoroethyl)pyrazol-4-yl]oxybenzonitrile
835		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[3-methyl-1-(2,2,2-trifluoroethyl)pyrazol-4-yl]oxybenzonitrile
836		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-methyl-1-(2,2,2-trifluoroethyl)pyrazol-4-yl]oxybenzonitrile
837		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-methyl-1-(2,2,2-trifluoroethyl)pyrazol-4-yl]oxybenzonitrile
838		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-[4-methoxybutyl (methyl)amino]-2-methylpyrazol-3 -yl]oxybenzonitrile
839		2-[[1-[6-[4-cyano-2-(2-methyl-5-pyridin-2-ylpyrazol-3 - yl) oxyphenyl]pyridin-3-yl]-2-methylpropan-2-yl]amino]-N,N-dimethylacetamide

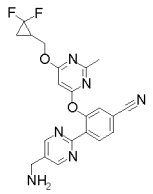
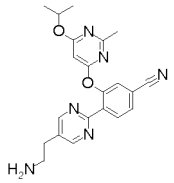
(continued)

Compound number	Structural formula	Compound name
840		2-[[1-[6-[4-cyano-2-(2-methyl-6-morpholin-4-ylpyridin-4-yl) oxyphenyl]pyridin-3-yl]-2-methylpropan-2-yl]amino]-N,N-dimethylacetamide

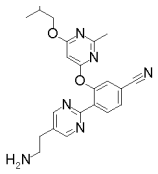
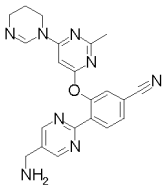
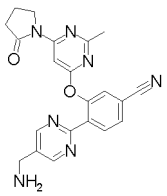
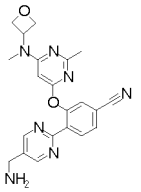
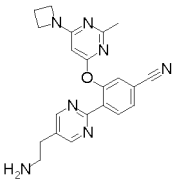
[Table 1-106]

Compound number	Structural formula	Compound name
841		2-[[2-[4-cyano-2-(2-methyl-6-pyridin-2-ylpyridin-4-yl) oxyphenyl]pyrimidin-5-yl]methylamino]acetamide
842		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-[ethyl(propan-2-yl)amino]-2-methylpyrazol-3 -yl]oxybenzonitrile
843		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(2-methoxyethoxy)-2-methylpyrimidin-4-yl]oxybenzonitrile
844		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-6-[(3R)-oxolan-3-yl]oxypyrimidin-4-yl]oxybenzonitrile
845		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-6-[(3 S)-oxolan-3-yl]oxypyrimidin-4-yl]oxybenzonitrile
846		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-6-(2-methylpropoxy)pyrimidin-4-yl]oxybenzonitrile

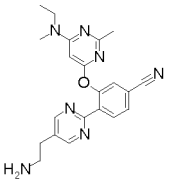
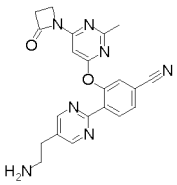
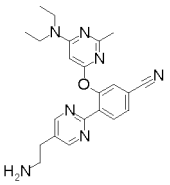
(continued)

Compound number	Structural formula	Compound name
847		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-[(2,2-difluorocyclopropyl)methoxy]-2-methylpyrimidin-4-yl] oxybenzonitrile
848		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-propan-2-yloxypyrimidin-4-yl)oxybenzonitrile

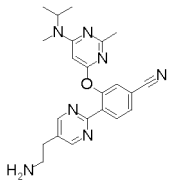
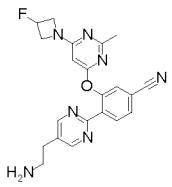
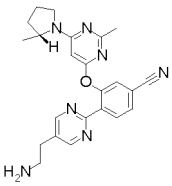
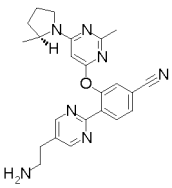
[Table 1-107]

Compound number	Structural formula	Compound name
849		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(2-methylpropoxy) pyrimidin-4-yl]oxybenzonitrile
850		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(5,6-dihydro-4H-pyrimidin-1-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile
851		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-6-(2-oxopyrrolidin-1-yl) pyrimidin-4-yl]oxybenzonitrile
852		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-6-[methyl(oxetan-3 - yl) amino]pyrimidin-4-yl]oxybenzonitrile
853		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[6-(azetidin-1-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile

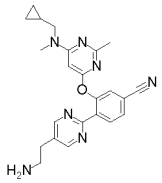
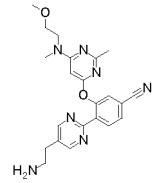
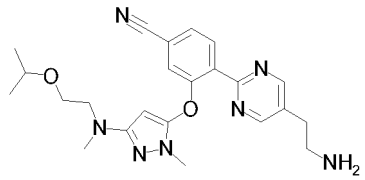
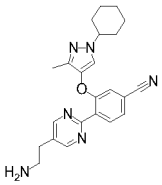
(continued)

Compound number	Structural formula	Compound name
854		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[6-[ethyl(methyl)amino]-2-methylpyrimidin-4-yl]oxybenzonitrile
855		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(2-oxoazetidin-1-yl)pyrimidin-4-yl]oxybenzonitrile
856		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[6-(diethylamino)-2-methylpyrimidin-4-yl]oxybenzonitrile

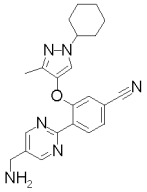
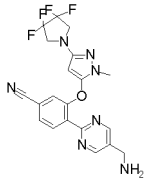
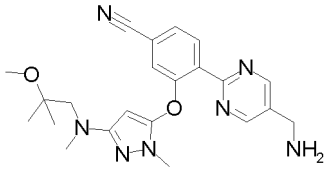
[Table 1-108]

Compound number	Structural formula	Compound name
857		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-[methyl(propan-2-yl)amino]pyrimidin-4-yl]oxybenzonitrile
858		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[6-(3-fluoroazetidin-1-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile
859		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-[(2R)-2-methylpyrrolidin-1-yl]pyrimidin-4-yl]oxybenzonitrile
860		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-[(2S)-2-methylpyrrolidin-1-yl]pyrimidin-4-yl]oxybenzonitrile

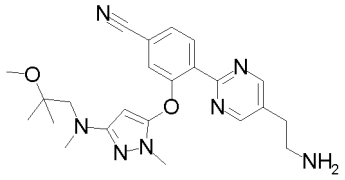
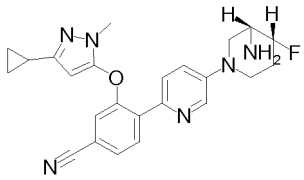
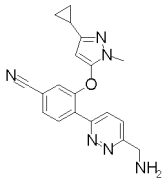
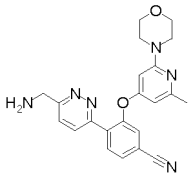
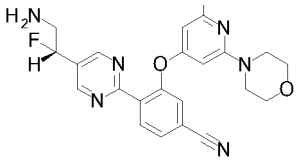
(continued)

Compound number	Structural formula	Compound name
861		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[6-[cyclopropylmethyl (methyl)amino]-2-methylpyrimidin-4-yl]oxybenzonitrile
862		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[6-[2-methoxyethyl (methyl)amino]-2-methylpyrimidin-4-yl]oxybenzonitrile
863		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-[methyl(2-propan-2-yloxyethyl)amino]pyrazol-3-yl]oxybenzonitrile
864		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(1-cyclohexyl-3-methylpyrazol-4-yl)oxybenzonitrile

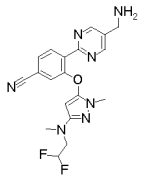
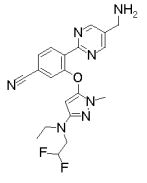
[Table 1-109]

Compound number	Structural formula	Compound name
865		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(1-cyclohexyl-3 -methylpyrazol-4-yl)oxybenzonitrile
866		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(3,3,4,4-tetrafluoropyrrolidin-1-yl)pyrazol-3-yl]oxybenzonitrile
867		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-[(2-methoxy-2-methylpropyl)-methylamino]-2-methylpyrazol-3-yl] oxybenzonitrile

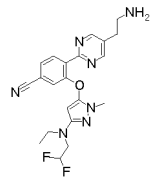
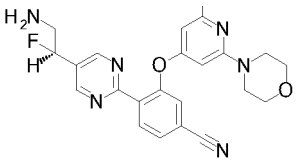
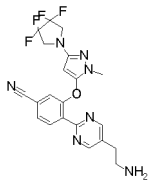
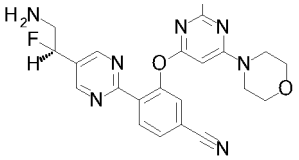
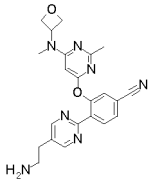
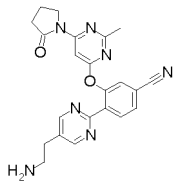
(continued)

Compound number	Structural formula	Compound name
868		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-[(2-methoxy-2-methylpropyl)-methylamino]-2-methylpyrazol-3-yl] oxybenzonitrile
869		4-[5-[(4R)-3-amino-4-fluoropiperidin-1-yl]pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
870		4-[6-(aminomethyl)pyridazin-3-yl]-3-(5-cyclopropyl-2-methylpyrazol-3 - yl)oxybenzonitrile
871		4-[6-(aminomethyl)pyridazin-3-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
872		4-[5-[(1S)-2-amino-1-fluoroethyl]pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile

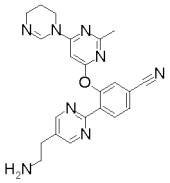
[Table 1-110]

Compound number	Structural formula	Compound name
873		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-[2,2-difluoroethyl (methyl)amino]-2-methylpyrazol-3 -yl]oxybenzonitrile
874		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-[2,2-difluoroethyl (ethyl)amino]-2-methylpyrazol-3-yl]oxybenzonitrile

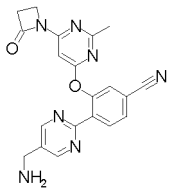
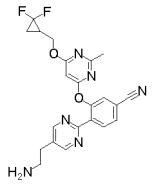
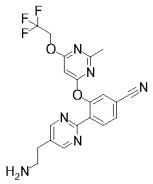
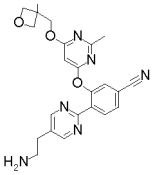
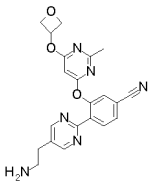
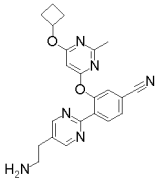
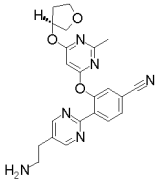
(continued)

Compound number	Structural formula	Compound name
875		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-[2,2-difluoroethyl (ethyl)amino]-2-methylpyrazol-3 -yl]oxybenzonitrile
876		4-[5-[(1R)-2-amino-1-fluoroethyl]pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
877		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-(3,3,4,4-tetrafluoropyrrolidin-1-yl)pyrazol-3-yl]oxybenzonitrile
878		4-[5-[(1R)-2-amino-1-fluoroethyl]pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
879		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-[methyl (oxetan-3- yl)amino]pyrimidin-4-yl]oxybenzonitrile
880		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(2-oxopyrrolidin-1-yl)pyrimidin-4-yl]oxybenzonitrile

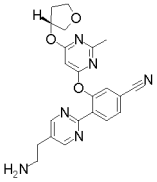
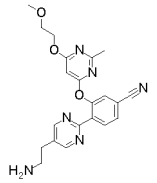
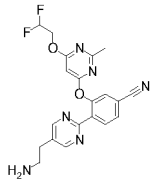
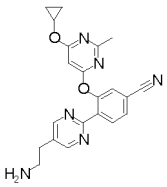
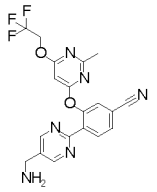
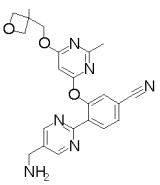
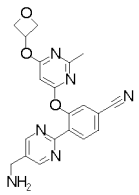
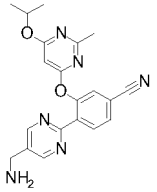
[Table 1-111]

Compound number	Structural formula	Compound name
881		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[6-(5,6-dihydro-4H-pyrimidin-1-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile

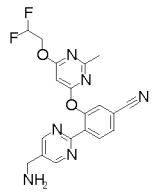
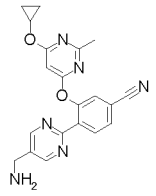
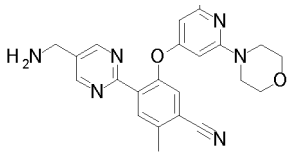
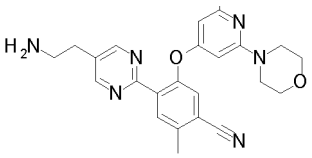
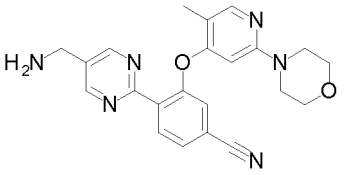
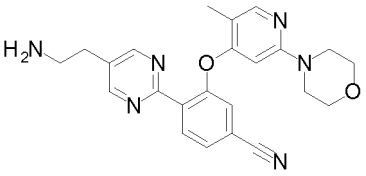
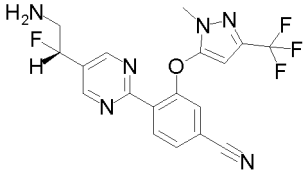
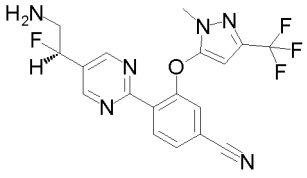
(continued)

Compound number	Structural formula	Compound name
882		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-6-(2-oxoazetidin-1-yl) pyrimidin-4-yl]oxybenzonitrile
883		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[6-[(2,2-difluorocyclopropyl) methoxy]-2-methylpyrimidin-4-yl]oxybenzonitrile
884		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(2,2,2-trifluoroethoxy) pyrimidin-4-yl]oxybenzonitrile
885		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-[(3-methyloxetan-3 - yl)methoxy]pyrimidin-4-yl]oxybenzonitrile
886		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(oxetan-3 - yloxy) pyrimidin-4-yl]oxybenzonitrile
887		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(6-cyclobutyloxy-2- methylpyrimidin-4-yl)oxybenzonitrile
888		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-[(3S)-oxolan-3-yl] oxypyrimidin-4-yl]oxybenzonitrile

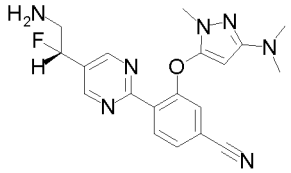
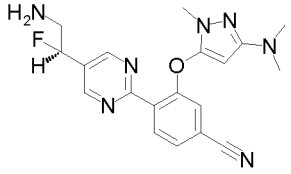
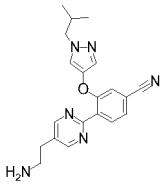
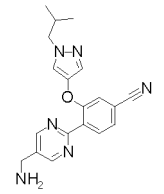
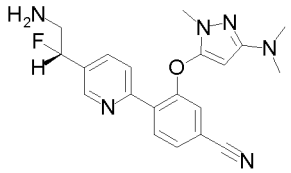
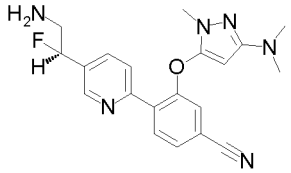
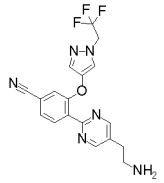
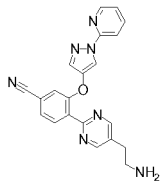
[Table 1-112]

Compound number	Structural formula	Compound name
889		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-[(3R)-oxolan-3-yl] oxypyrimidin-4-yl]oxybenzonitrile
890		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[6-(2-methoxyethoxy)-2-methylpyrimidin-4-yl]oxybenzonitrile
891		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[6-(2,2-difluoroethoxy)-2-methylpyrimidin-4-yl]oxybenzonitrile
892		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(6-cyclopropyloxy-2-methylpyrimidin-4-yl)oxybenzonitrile
893		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-6-(2,2,2-trifluoroethoxy) pyrimidin-4-yl]oxybenzonitrile
894		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-6-[(3-methyloxetan-3-yl) methoxy]pyrimidin-4-yl]oxybenzonitrile
895		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-6-(oxetan-3- yloxy) pyrimidin-4-yl]oxybenzonitrile
896		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-6-propan-2-yloxypyrimidin-4-yl)oxybenzonitrile

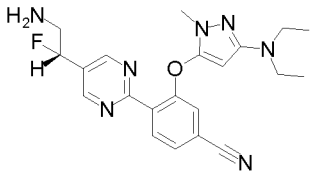
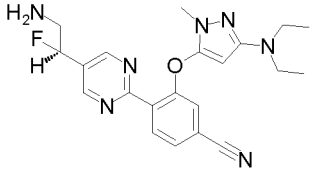
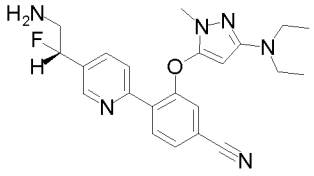
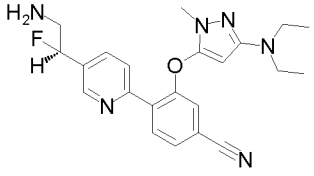
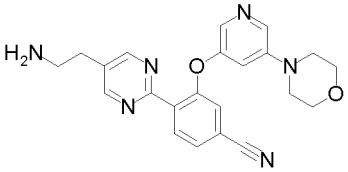
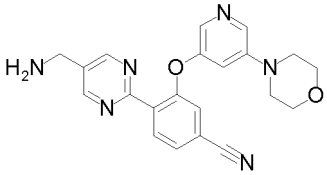
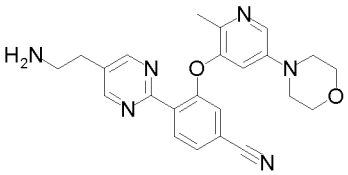
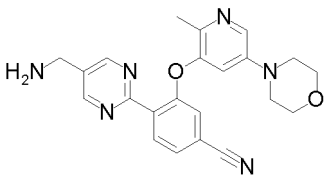
[Table 1-113]

Compound number	Structural formula	Compound name
897		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(2,2-difluoroethoxy)-2-methylpyrimidin-4-yl] oxybenzonitrile
898		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(6-cyclopropyloxy-2-methylpyrimidin-4-yl) oxybenzonitrile
899		4-[5-(aminomethyl)pyrimidin-2-yl]-2-methyl-5-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
900		4-[5-(2-aminoethyl)pyrimidin-2-yl]-2-methyl-5-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
901		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(5-methyl-2-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
902		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-methyl-2-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
903		4-[5-[(1S)-2-amino-1-fluoroethyl]pyrimidin-2-yl]-3-[2-methyl-5-(trifluoromethyl)pyrazol-3-yl] oxybenzonitrile
904		4-[5-[(1R)-2-amino-1-fluoroethyl]pyrimidin-2-yl]-3-[2-methyl-5-(trifluoromethyl)pyrazol-3-yl] oxybenzonitrile

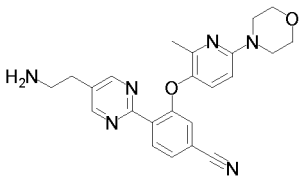
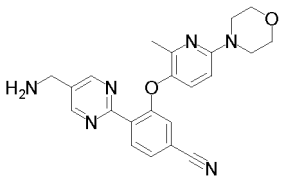
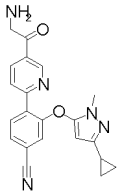
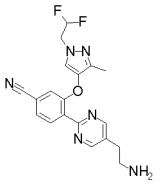
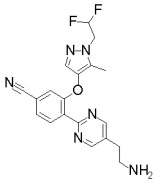
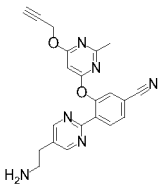
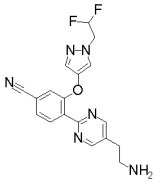
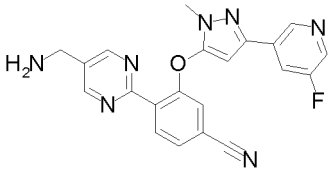
[Table 1-114]

Compound number	Structural formula	Compound name
905		4-[5-[(1S)-2-amino-1-fluoroethyl]pyrimidin-2-yl]-3-[5-(dimethylamino)-2-methylpyrazol-3-yl]oxybenzonitrile
906		4-[5-[(1R)-2-amino-1-fluoroethyl]pyrimidin-2-yl]-3-[5-(dimethylamino)-2-methylpyrazol-3 - yl]oxybenzonitrile
907		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[1-(2-methylpropyl)pyrazol-4-yl]oxybenzonitrile
908		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[1-(2-methylpropyl)pyrazol-4-yl]oxybenzonitrile
909		4-[5-[(1S)-2-amino-1-fluoroethyl]pyridin-2-yl]-3-[5-(dimethylamino)-2-methylpyrazol-3-yl]oxybenzonitrile
910		4-[5-[(1R)-2-amino-1-fluoroethyl]pyridin-2-yl]-3-[5-(dimethylamino)-2-methylpyrazol-3 - yl]oxybenzonitrile
911		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[1-(2,2,2-trifluoroethyl) pyrazol-4-yl]oxybenzonitrile
912		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(1-pyridin-2-ylpyrazol-4-yl) oxybenzonitrile

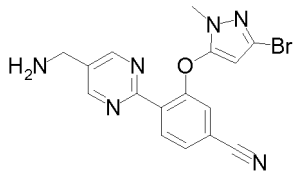
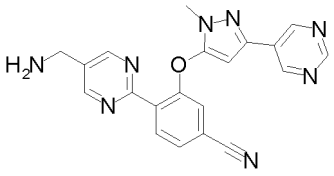
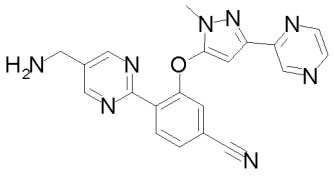
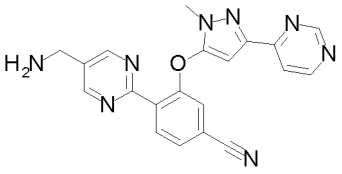
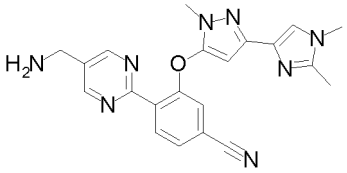
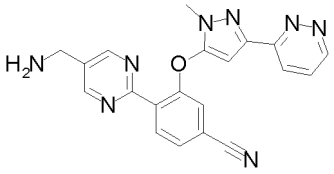
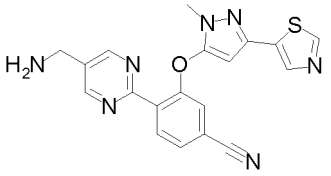
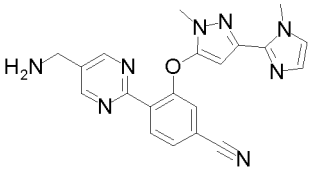
[Table 1-115]

Compound number	Structural formula	Compound name
913		4-[5-[(1S)-2-amino-1-fluoroethyl]pyrimidin-2-yl]-3-[5-(diethylamino)-2-methylpyrazol-3-yl] oxybenzonitrile
914		4-[5-[(1R)-2-amino-1-fluoroethyl]pyrimidin-2-yl]-3-[5-(diethylamino)-2-methylpyrazol-3-yl] oxybenzonitrile
915		4-[5-[(1S)-2-amino-1-fluoroethyl]pyridin-2-yl]-3-[5-(diethylamino)-2-methylpyrazol-3-yl] oxybenzonitrile
916		4-[5-[(1R)-2-amino-1-fluoroethyl]pyridin-2-yl]-3-[5-(diethylamino)-2-methylpyrazol-3-yl] oxybenzonitrile
917		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-morpholin-4-ylpyridin-3 - yl)oxybenzonitrile
918		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(5-morpholin-4-ylpyridin-3 - yl)oxybenzonitrile
919		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-morpholin-4-ylpyridin-3-yl)oxybenzonitrile
920		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-morpholin-4-ylpyridin-3-yl)oxybenzonitrile

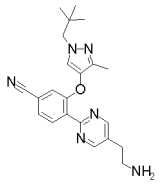
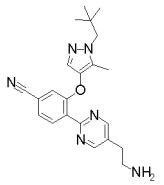
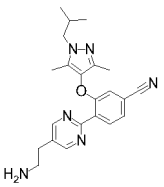
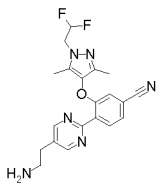
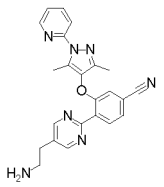
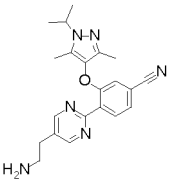
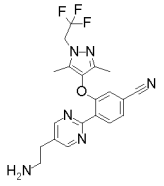
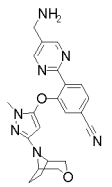
[Table 1-116]

Compound number	Structural formula	Compound name
921		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-3 - yl)oxybenzonitrile
922		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-3 - yl)oxybenzonitrile
923		4-[5-(2-aminoacetyl)pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3 - yl)oxybenzonitrile
924		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[1-(2,2-difluoroethyl)-3-methylpyrazol-4-yl]oxybenzonitrile
925		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[1-(2,2-difluoroethyl)-5-methylpyrazol-4-yl]oxybenzonitrile
926		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-prop-2-ynoxypyrimidin-4-yl)oxybenzonitrile
927		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[1-(2,2-difluoroethyl)pyrazol-4-yl]oxybenzonitrile
928		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-(5-fluoropyridin-3-yl)-2-methylpyrazol-3-yl]oxybenzonitrile

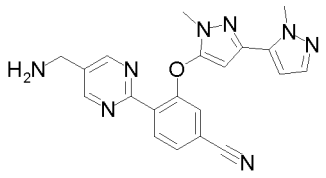
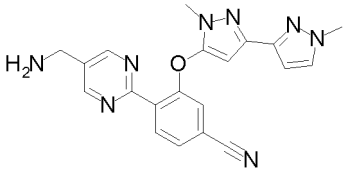
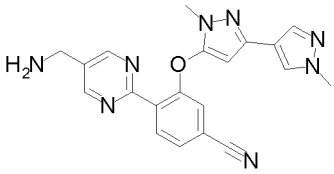
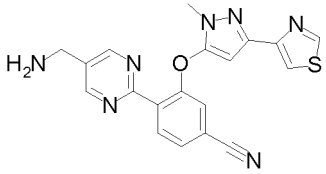
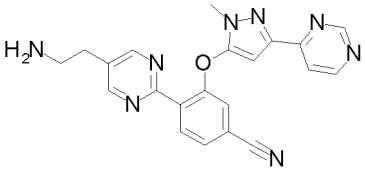
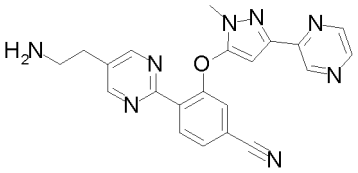
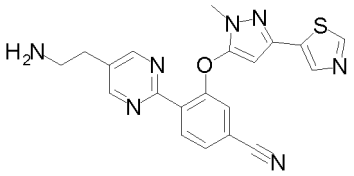
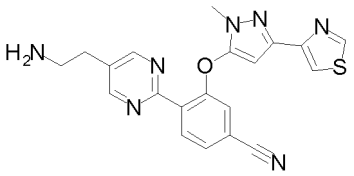
[Table 1-117]

Compound number	Structural formula	Compound name
929		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(5-bromo-2-methylpyrazol-3- yl)oxybenzonitrile
930		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-pyrimidin-5-ylpyrazol-3-yl)oxybenzonitrile
931		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-pyrazin-2-ylpyrazol-3-yl)oxybenzonitrile
932		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-pyrimidin-4-ylpyrazol-3-yl)oxybenzonitrile
933		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-(1,2-dimethylimidazol-4-yl)-2-methylpyrazol-3-yl] oxybenzonitrile
934		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-pyridazin-3-ylpyrazol-3-yl)oxybenzonitrile
935		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(1,3-thiazol-5-yl)pyrazol-3-yl]oxybenzonitrile
936		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(1-methylimidazol-2-yl)pyrazol-3-yl]oxybenzonitrile

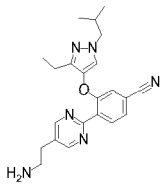
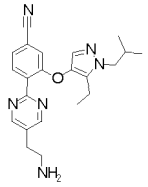
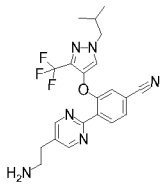
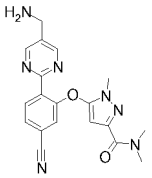
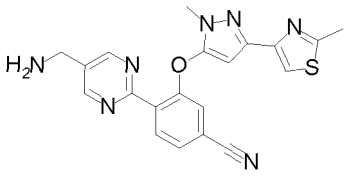
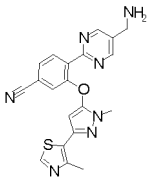
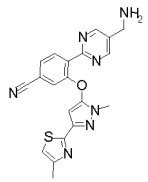
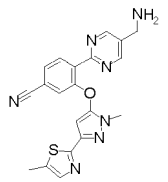
[Table 1-118]

Compound number	Structural formula	Compound name
937		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[1-(2,2-dimethylpropyl)-3-methylpyrazol-4-yl]oxybenzonitrile
938		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[1-(2,2-dimethylpropyl)-5-methylpyrazol-4-yl]oxybenzonitrile
939		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[3,5-dimethyl-1-(2-methylpropyl) pyrazol-4-yl]oxybenzonitrile
940		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[1-(2,2-difluoroethyl)-3,5-dimethylpyrazol-4-yl]oxybenzonitrile
941		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(3,5-dimethyl-1-pyridin-2-ylpyrazo-4-yl)oxybenzonitrile
942		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(3,5-dimethyl-1-propan-2-ylpyrazol-4-yl)oxybenzonitrile
943		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[3,5-dimethyl-1-(2,2,2-trifluoroethyl)pyrazol-4-yl]oxybenzonitrile
944		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(3-oxa-8-azabicyclo [3.2.1]octan-8-yl)pyrazol-3-yl]oxybenzonitrile

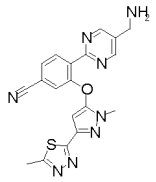
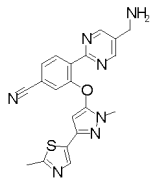
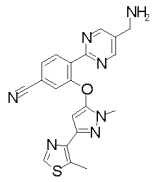
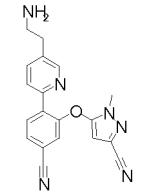
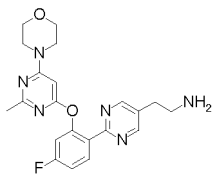
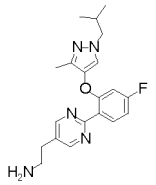
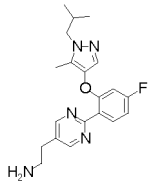
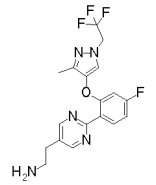
[Table 1-119]

Compound number	Structural formula	Compound name
945		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(2-methylpyrazol-3-yl)pyrazol-3-yl]oxybenzonitrile
946		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(1-methylpyrazol-3-yl)pyrazol-3-yl]oxybenzonitrile
947		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(1-methylpyrazol-4-yl)pyrazol-3-yl]oxybenzonitrile
948		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(1,3 -thiazol-4-yl)pyrazol-3-yl]oxybenzonitrile
949		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-pyrimidin-4-ylpyrazol-3-yl)oxybenzonitrile
950		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-pyrazin-2-ylpyrazol-3-yl)oxybenzonitrile
951		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-(1,3-thiazol-5-yl)pyrazol-3-yl]oxybenzonitrile
952		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-(1,3-thiazol-4-yl)pyrazol-3-yl]oxybenzonitrile

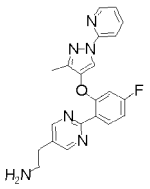
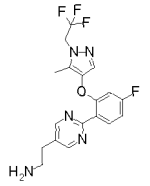
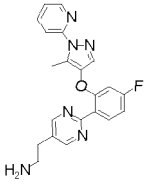
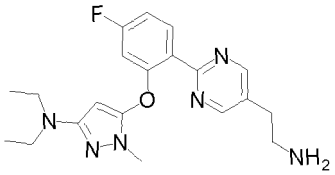
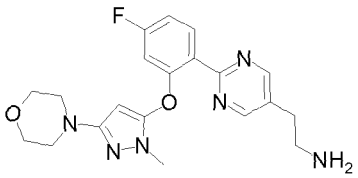
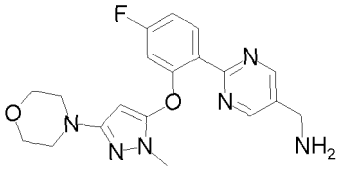
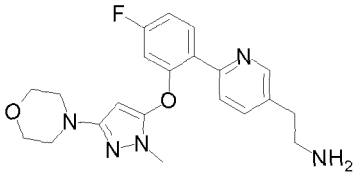
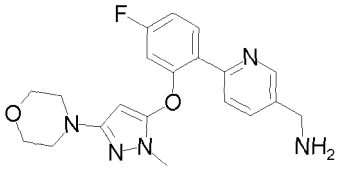
[Table 1-120]

Compound number	Structural formula	Compound name
953		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[3-ethyl-1-(2-methylpropyl)pyrazol-4-yl]oxybenzonitrile
954		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-ethyl-1-(2-methylpropyl)pyrazol-4-yl]oxybenzonitrile
955		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[1-(2-methylpropyl)-3-(trifluoromethyl)pyrazol-4-yl]oxybenzonitrile
956		5-[2-[5-(aminomethyl)pyrimidin-2-yl]-5-cyanophenoxy]-N,N,1-trimethylpyrazole-3 -carboxamide
957		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(2-methyl-1,3-thiazol-4-yl)pyrazol-3-yl]oxybenzonitrile
958		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(4-methyl-1,3-thiazol-5-yl)pyrazol-3-yl]oxybenzonitrile
959		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(4-methyl-1,3-thiazol-2-yl)pyrazol-3-yl]oxybenzonitrile
960		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(5-methyl-1,3-thiazol-2-yl)pyrazol-3-yl]oxybenzonitrile

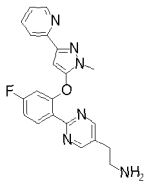
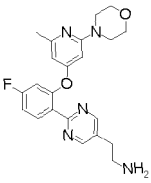
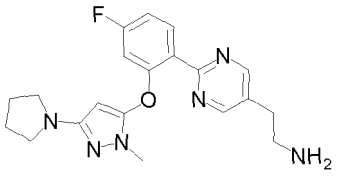
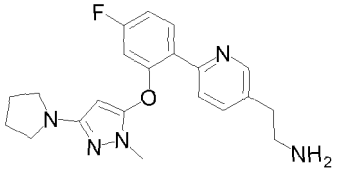
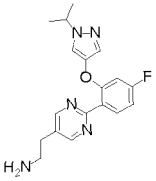
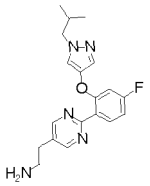
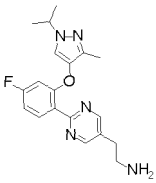
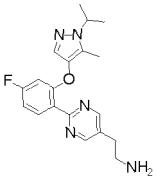
[Table 1-121]

Compound number	Structural formula	Compound name
961		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(5-methyl-1,3,4-thiadiazol-2-yl)pyrazol-3-yl]oxybenzonitrile
962		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(2-methyl-1,3-thiazol-5-yl)pyrazol-3 -yl]oxybenzonitrile
963		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(5-methyl-1,3-thiazol-4-yl)pyrazol-3-yl]oxybenzonitrile
964		5-[2-[5-(2-aminoethyl)pyridin-2-yl]-5-cyanophenoxy]-1-methylpyrazole-3-carbonitrile
965		2-[2-[4-fluoro-2-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl) oxyphenyl]pyrimidin-5-yl]ethanamine
966		2-[2-[4-fluoro-2-[3-methyl-1-(2-methylpropyl)pyrazol-4-yl] oxyphenyl]pyrimidin-5-yl]ethanamine
967		2-[2-[4-fluoro-2-[5-methyl-1-(2-methylpropyl)pyrazol-4-yl] oxyphenyl]pyrimidin-5-yl]ethanamine
968		2-[2-[4-fluoro-2-[3-methyl-1-(2,2,2-trifluoroethyl)pyrazol-4-yl] oxyphenyl]pyrimidin-5-yl]ethanamine

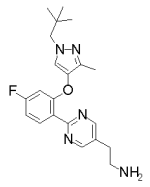
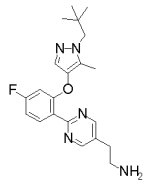
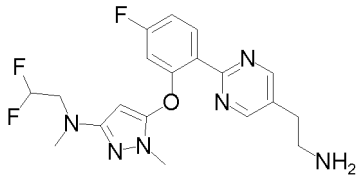
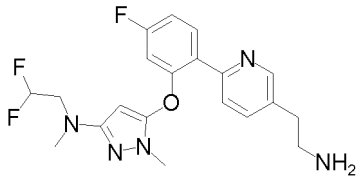
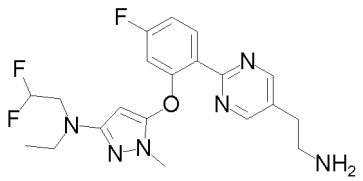
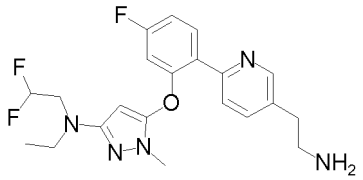
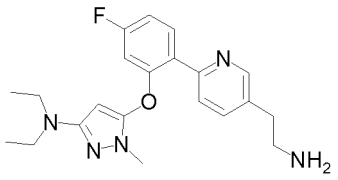
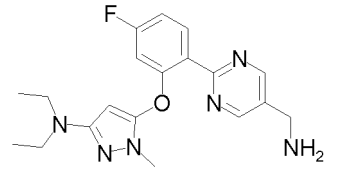
[Table 1-122]

Compound number	Structural formula	Compound name
969		2-[2-[4-fluoro-2-(3-methyl-1-pyridin-2-ylpyrazol-4-yl) oxyphenyl]pyrimidin-5-yl]ethanamine
970		2-[2-[4-fluoro-2-[5-methyl-1-(2,2,2-trifluoroethyl) pyrazol-4-yl]oxyphenyl]pyrimidin-5-yl]ethanamine
971		2-[2-[4-fluoro-2-(5-methyl-1-pyridin-2-ylpyrazol-4-yl) oxyphenyl]pyrimidin-5-yl]ethanamine
972		5-[2-[5-(2-aminoethyl)pyrimidin-2-yl]-5-fluorophenoxy]-N,N-diethyl-1-methyl pyrazole-3 -amine
973		2-[2-[4-fluoro-2-(2-methyl-5-morpholin-4-ylpyrazol-3-yl)oxyphenyl]pyrimidin-5-yl]ethanamine
974		[2-[4-fluoro-2-(2-methyl-5-morpholin-4-ylpyrazol-3-yl)oxyphenyl]pyrimidin-5-yl]methanamine
975		2-[6-[4-fluoro-2-(2-methyl-5-morpholin-4-ylpyrazol-3-yl)oxyphenyl]pyridin-3 - yl]ethanamine
976		[6-[4-fluoro-2-(2-methyl-5-morpholin-4-ylpyrazol-3-yl)oxyphenyl]pyridin-3 - yl]methanamine

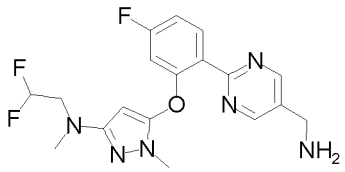
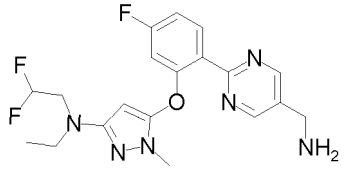
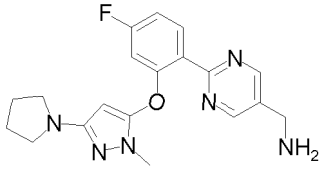
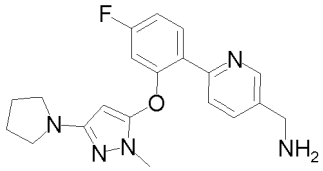
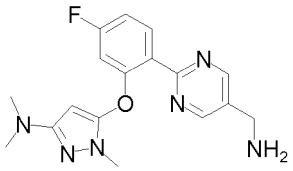
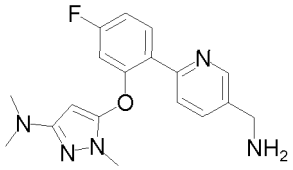
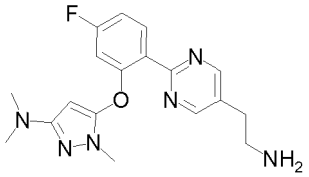
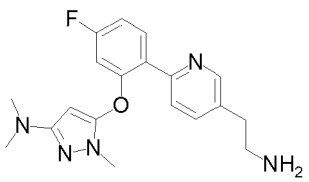
[Table 1-123]

Compound number	Structural formula	Compound name
977		2-[2-[4-fluoro-2-(2-methyl-5-pyridin-2-ylpyrazol-3-yl) oxyphenyl]pyrimidin-5-yl]ethanamine
978		2-[2-[4-fluoro-2-(2-methyl-6-morpholin-4-ylpyridin-4-yl) oxyphenyl]pyrimidin-5-yl]ethanamine
979		2-[2-[4-fluoro-2-(2-methyl-5-pyrrolidin-1-ylpyrazol-3-yl) oxyphenyl]pyrimidin-5-yl]ethanamine
980		2-[6-[4-fluoro-2-(2-methyl-5-pyrrolidin-1-ylpyrazol-3-yl) oxyphenyl]pyridin-3-yl]ethanamine
981		2-[2-[4-fluoro-2-(1-propan-2-ylpyrazol-4-yl)oxyphenyl] pyrimidin-5-yl]ethanamine
982		2-[2-[4-fluoro-2-[1-(2-methylpropyl)pyrazol-4-yl] oxyphenyl]pyrimidin-5-yl]ethanamine
983		2-[2-[4-fluoro-2-(3-methyl-1-propan-2-ylpyrazol-4-yl) oxyphenyl]pyrimidin-5-yl]ethanamine
984		2-[2-[4-fluoro-2-(5-methyl-1-propan-2-ylpyrazol-4-yl) oxyphenyl]pyrimidin-5-yl]ethanamine

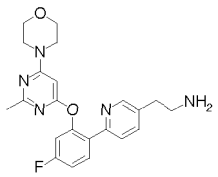
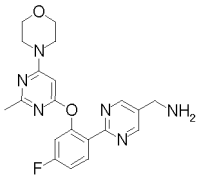
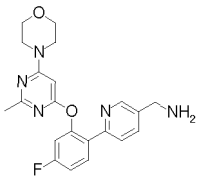
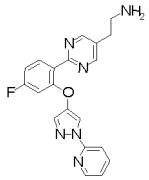
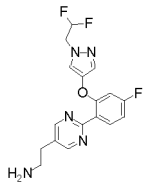
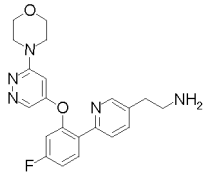
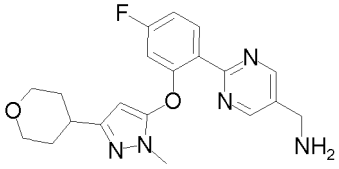
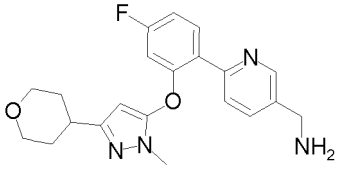
[Table 1-124]

Compound number	Structural formula	Compound name
985		2-[2-[2-[1-(2,2-dimethylpropyl)-3-methylpyrazol-4-yl]oxy-4-fluorophenyl]pyrimidin-5-yl]ethanamine
986		2-[2-[2-[1-(2,2-dimethylpropyl)-5-methylpyrazol-4-yl]oxy-4-fluorophenyl]pyrimidin-5-yl]ethanamine
987		5-[2-[5-(2-aminoethyl)pyrimidin-2-yl]-5-fluorophenoxy]-N-(2,2-difluoroethyl)-N,1-dimethylpyrazole-3-amine
988		5-[2-[5-(2-aminoethyl)pyridin-2-yl]-5-fluorophenoxy]-N-(2,2-difluoroethyl)-N,1-dimethylpyrazole-3-amine
989		5-[2-[5-(2-aminoethyl)pyrimidin-2-yl]-5-fluorophenoxy]-N-(2,2-difluoroethyl)-N-ethyl-1-methylpyrazole-3 -amine
990		5-[2-[5-(2-aminoethyl)pyridin-2-yl]-5-fluorophenoxy]-N-(2,2-difluoroethyl)-N-ethyl-1-methylpyrazole-3 -amine
991		5-[2-[5-(2-aminoethyl)pyridin-2-yl]-5-fluorophenoxy]-N,N-diethyl-1-methylpyrazole-3 -amine
992		5-[2-[5-(aminomethyl)pyrimidin-2-yl]-5-fluorophenoxy]-N,N-diethyl-1-methylpyrazole-3-amine

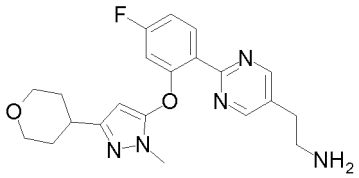
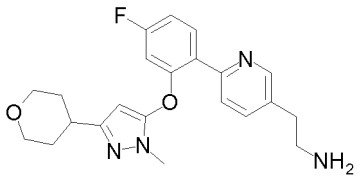
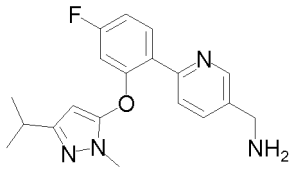
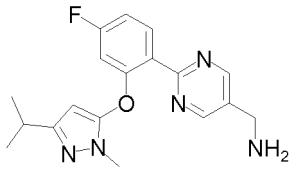
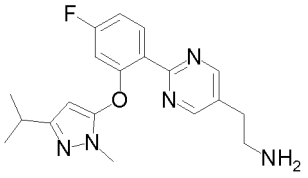
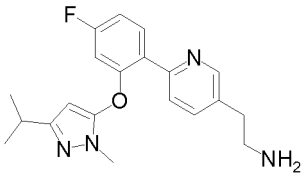
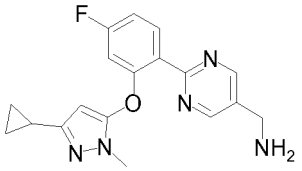
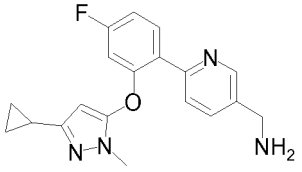
[Table 1-125]

Compound number	Structural formula	Compound name
993		5-[2-[5-(aminomethyl)pyrimidin-2-yl]-5-fluorophenoxy]-N-(2,2-difluoroethyl)-N,1-dimethylpyrazole-3-amine
994		5-[2-[5-(aminomethyl)pyrimidin-2-yl]-5-fluorophenoxy]-N-(2,2-difluoroethyl)-N-ethyl-1-methylpyrazole-3 -amine
995		[2-[4-fluoro-2-(2-methyl-5-pyrrolidin-1-ylpyrazol-3-yl) oxyphenyl]pyrimidin-5-yl]methanamine
996		[6-[4-fluoro-2-(2-methyl-5-pyrrolidin-1-ylpyrazol-3-yl) oxyphenyl]pyridin-3 - yl]methanamine
997		5-[2-[5-(aminomethyl)pyrimidin-2-yl]-5-fluorophenoxy]-N,N, 1- trimethylpyrazole-3-amine
998		5-[2-[5-(aminomethyl)pyridin-2-yl]-5-fluorophenoxy]-N,N,1-trimethylpyrazole-3-amine
999		5-[2-[5-(2-aminoethyl)pyrimidin-2-yl]-5-fluorophenoxy]-N,N, 1-trimethylpyrazole-3-amine
1000		5-[2-[5-(2-aminoethyl)pyridin-2-yl]-5-fluorophenoxy]-N,N,1-trimethylpyrazole-3-amine

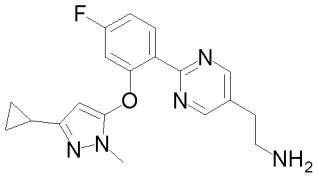
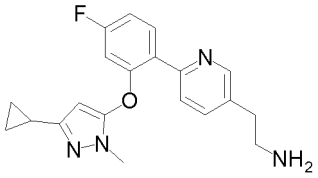
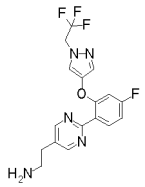
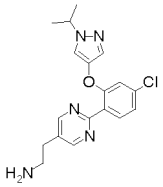
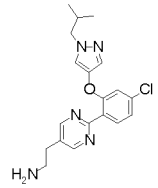
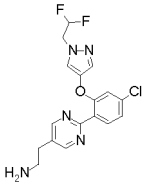
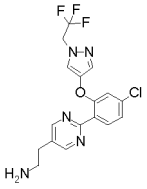
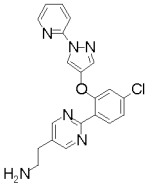
[Table 1-126]

Compound number	Structural formula	Compound name
1001		2-[6-[4-fluoro-2-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxyphenyl]pyridin-3-yl]ethanamine
1002		[2-[4-fluoro-2-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxyphenyl]pyrimidin-5-yl]methanamine
1003		[6-[4-fluoro-2-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxyphenyl]pyridin-3-yl]methanamine
1004		2-[2-[4-fluoro-2-(1-pyridin-2-ylpyrazol-4-yl)oxyphenyl] pyrimidin-5-yl]ethanamine
1005		2-[2-[2-[1-(2,2-difluoroethyl)pyrazol-4-yl]oxy-4-fluorophenyl]pyrimidin-5-yl]ethanamine
1006		2-[6-[4-fluoro-2-(6-morpholin-4-ylpyridazin-4-yl) oxyphenyl]pyridin-3-yl]ethanamine
1007		[2-[4-fluoro-2-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl] oxyphenyl]pyrimidin-5-yl]methanamine
1008		[6-[4-fluoro-2-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl] oxyphenyl]pyridin-3- yl]methanamine

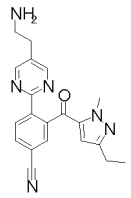
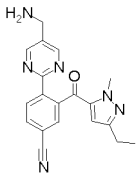
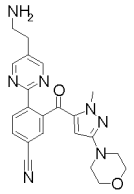
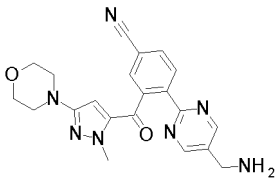
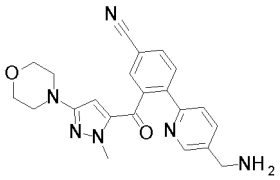
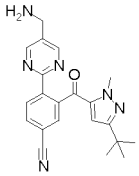
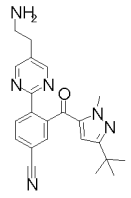
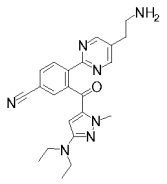
[Table 1-127]

Compound number	Structural formula	Compound name
1009		2-[2-[4-fluoro-2-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl] oxyphenyl]pyrimidin-5-yl]ethanamine
1010		2-[6-[4-fluoro-2-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl] oxyphenyl]pyridin-3-yl]ethanamine
1011		[6-[4-fluoro-2-(2-methyl-5-propan-2-ylpyrazol-3-yl) oxyphenyl]pyridin-3-yl]methanamine
1012		[2-[4-fluoro-2-(2-methyl-5-propan-2-ylpyrazol-3-yl) oxyphenyl]pyrimidin-5-yl]methanamine
1013		2-[2-[4-fluoro-2-(2-methyl-5-propan-2-ylpyrazol-3-yl) oxyphenyl]pyrimidin-5-yl]ethanamine
1014		2-[6-[4-fluoro-2-(2-methyl-5-propan-2-ylpyrazol-3-yl) oxyphenyl]pyridin-3-yl]ethanamine
1015		[2-[2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxy-4-fluorophenyl]pyrimidin-5-yl]methanamine
1016		[6-[2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxy-4-fluorophenyl]pyridin-3-yl]methanamine

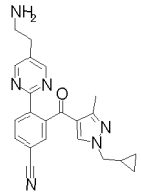
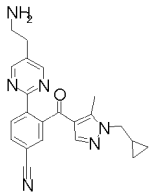
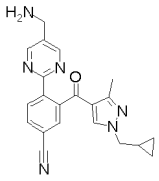
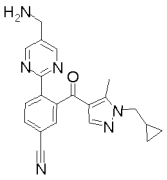
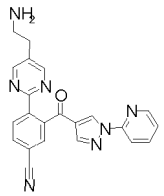
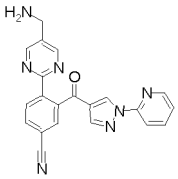
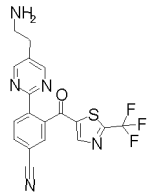
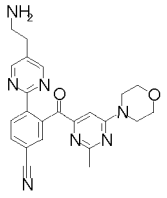
[Table 1-128]

Compound number	Structural formula	Compound name
1017		2-[2-[2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxy-4-fluorophenyl]pyrimidin-5-yl]ethanamine
1018		2-[6-[2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxy-4-fluorophenyl]pyridin-3-yl]ethanamine
1019		2-[2-[4-fluoro-2-[1-(2,2,2-trifluoroethyl)pyrazol-4-yl]oxyphenyl]pyrimidin-5-yl]ethanamine
1020		2-[2-[4-chloro-2-(1-propan-2-ylpyrazol-4-yl)oxyphenyl]pyrimidin-5-yl]ethanamine
1021		2-[2-[4-chloro-2-[1-(2-methylpropyl)pyrazol-4-yl]oxyphenyl]pyrimidin-5-yl]ethanamine
1022		2-[2-[4-chloro-2-[1-(2,2-difluoroethyl)pyrazol-4-yl]oxyphenyl]pyrimidin-5-yl]ethanamine
1023		2-[2-[4-chloro-2-[1-(2,2,2-trifluoroethyl)pyrazol-4-yl]oxyphenyl]pyrimidin-5-yl]ethanamine
1024		2-[2-[4-chloro-2-(1-pyridin-2-ylpyrazol-4-yl)oxyphenyl]pyrimidin-5-yl]ethanamine

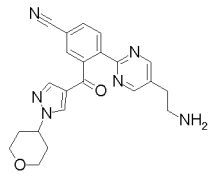
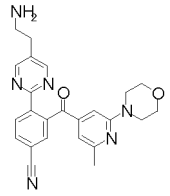
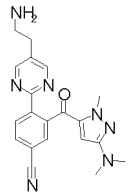
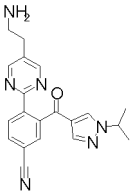
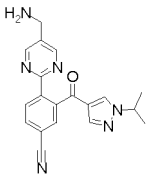
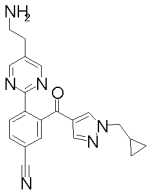
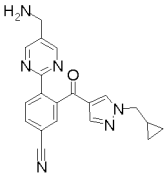
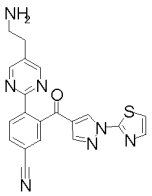
[Table 1-129]

Compound number	Structural formula	Compound name
1025		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-ethyl-2-methylpyrazole-3-carbonyl)benzonitrile
1026		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(5-ethyl-2-methylpyrazole-3-carbonyl)benzonitrile
1027		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-morpholin-4-ylpyrazole-3-carbonyl)benzonitrile
1028		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-morpholin-4-ylpyrazole-3-carbonyl)benzonitrile
1029		4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-5-morpholin-4-ylpyrazole-3-carbonyl)benzonitrile
1030		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(5-tert-butyl-2-methylpyrazole-3-carbonyl)benzonitrile
1031		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-tert-butyl-2-methylpyrazole-3-carbonyl)benzonitrile
1032		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-(diethylamino)-2-methylpyrazole-3-carbonyl]benzonitrile

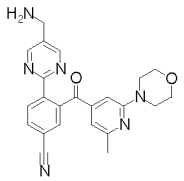
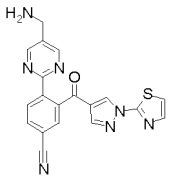
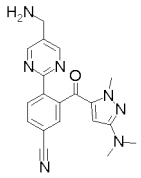
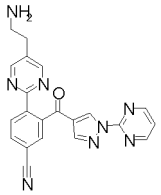
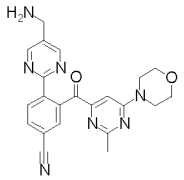
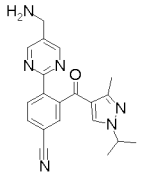
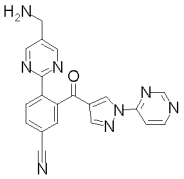
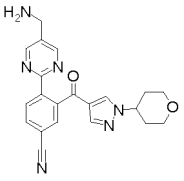
[Table 1-130]

Compound number	Structural formula	Compound name
1033		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[1-(cyclopropylmethyl)-3 -methylpyrazole-4-carbonyl]benzonitrile
1034		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[1-(cyclopropylmethyl)-5-methylpyrazole-4-carbonyl]benzonitrile
1035		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[1-(cyclopropylmethyl)-3 -methylpyrazole-4-carbonyl]benzonitrile
1036		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[1-(cyclopropylmethyl)-5-methylpyrazole-4-carbonyl]benzonitrile
1037		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(1-pyridin-2-ylpyrazole-4-carbonyl) benzonitrile
1038		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(1-pyridin-2-ylpyrazole-4-carbonyl) benzonitrile
1039		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-(trifluoromethyl)-1,3 -thiazole-5-carbonyl]benzonitrile
1040		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyrimidine-4-carbonyl)benzonitrile

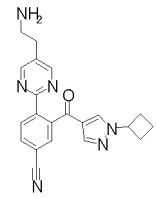
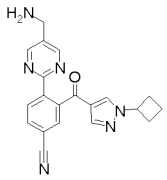
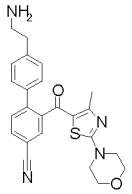
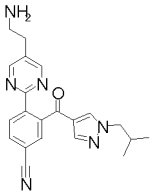
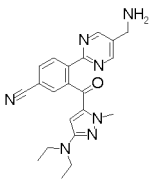
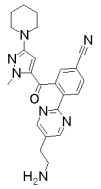
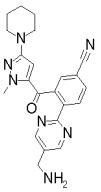
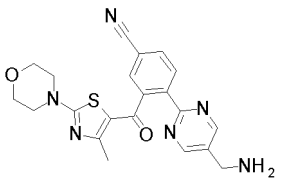
[Table 1-131]

Compound number	Structural formula	Compound name
1041		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[1-(oxan-4-yl)pyrazole-4-carbonyl]benzonitrile
1042		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridine-4-carbonyl)benzonitrile
1043		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-(dimethylamino)-2-methylpyrazole-3-carbonyl]benzonitrile
1044		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(1-prop an-2-ylpyrazole-4-carbonyl)benzonitrile
1045		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(1-prop an-2-ylpyrazole-4-carbonyl)benzonitrile
1046		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[1-(cyclopropylmethyl)pyrazole-4-carbonyl]benzonitrile
1047		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[1-(cyclopropylmethyl)pyrazole-4-carbonyl]benzonitrile
1048		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[1-(1,3-thiazol-2-yl)pyrazole-4-carbonyl]benzonitrile

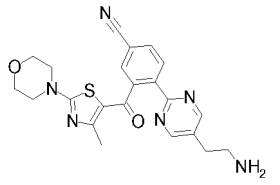
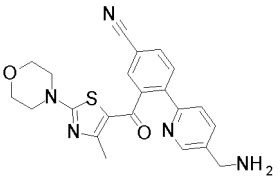
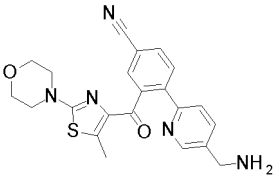
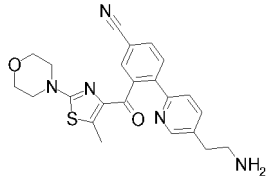
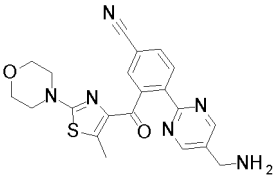
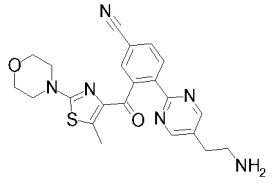
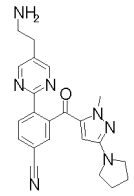
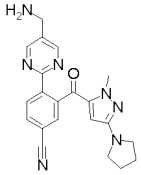
[Table 1-132]

Compound number	Structural formula	Compound name
1049		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridine-4-carbonyl)benzonitrile
1050		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[1-(1,3-thiazol-2-yl)pyrazole-4-carbonyl]benzonitrile
1051		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-(dimethylamino)-2-methylpyrazole-3-carbonyl]benzonitrile
1052		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(1-pyrimidin-2-ylpyrazole-4-carbonyl)benzonitrile
1053		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyrimidine-4-carbonyl)benzonitrile
1054		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(3-methyl-1-propan-2-ylpyrazole-4-carbonyl)benzonitrile
1055		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(1-pyrimidin-4-ylpyrazole-4-carbonyl)benzonitrile
1056		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[1-(oxan-4-yl)pyrazole-4-carbonyl]benzonitrile

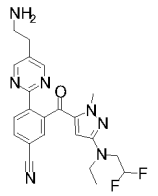
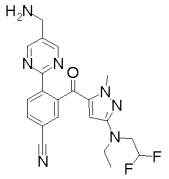
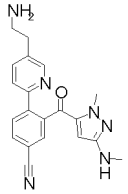
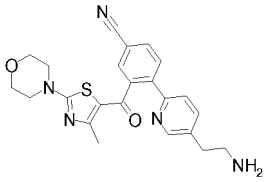
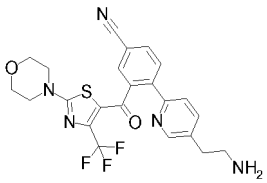
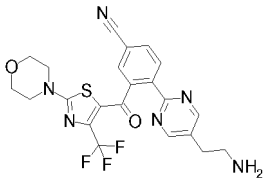
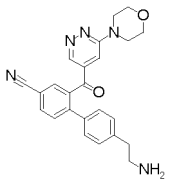
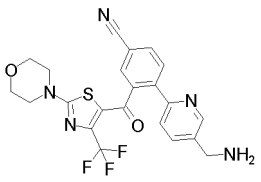
[Table 1-133]

Compound number	Structural formula	Compound name
1057		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(1-cyclobutylpyrazole-4-carbonyl)benzonitrile
1058		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(1-cyclobutylpyrazole-4-carbonyl)benzonitrile
1059		4-[4-(2-aminoethyl)phenyl]-3-(4-methyl-2-morpholin-4-yl-1,3-thiazole-5-carbonyl)benzonitrile
1060		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[1-(2-methylpropyl) pyrazole-4-carbonyl]benzonitrile
1061		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-(diethylamino)-2-methylpyrazole-3-carbonyl]benzonitrile
1062		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-piperidin-1-ylpyrazole-3-carbonyl)benzonitrile
1063		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-piperidin-1-ylpyrazole-3-carbonyl)benzonitrile
1064		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(4-methyl-2-morpholin-4-yl-1,3-thiazole-5-carbonyl)benzonitrile

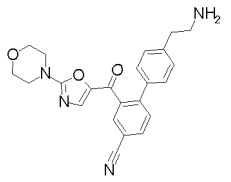
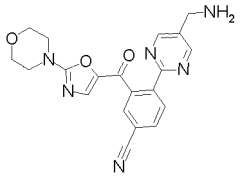
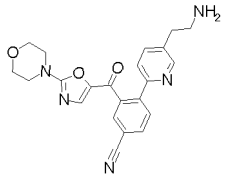
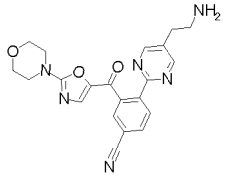
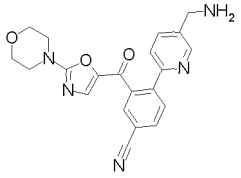
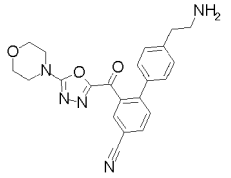
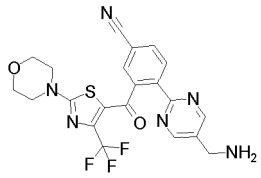
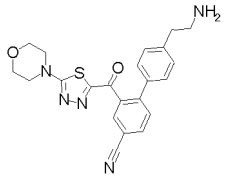
[Table 1-134]

Compound number	Structural formula	Compound name
1065		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(4-methyl-2-morpholin-4-yl-1,3-thiazole-5-carbonyl)benzonitrile
1066		4-[5-(aminomethyl)pyridin-2-yl]-3-(4-methyl-2-morpholin-4-yl-1,3-thiazole-5-carbonyl)benzonitrile
1067		4-[5-(aminomethyl)pyridin-2-yl]-3-(5-methyl-2-morpholin-4-yl-1,3-thiazole-4-carbonyl)benzonitrile
1068		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(5-methyl-2-morpholin-4-yl-1,3-thiazole-4-carbonyl)benzonitrile
1069		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(5-methyl-2-morpholin-4-yl-1,3-thiazole-4-carbonyl)benzonitrile
1070		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-methyl-2-morpholin-4-yl-1,3-thiazole-4-carbonyl)benzonitrile
1071		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-pyrrolidin-1-ylpyrazole-3-carbonyl)benzonitrile
1072		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-pyrrolidin-1-ylpyrazole-3-carbonyl)benzonitrile

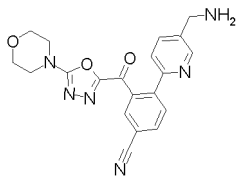
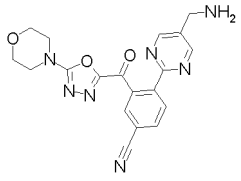
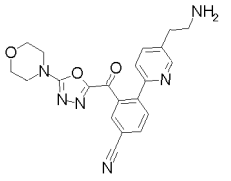
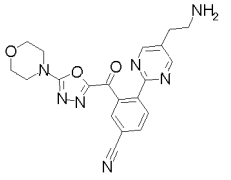
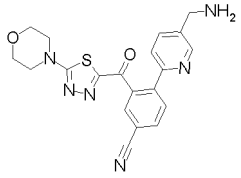
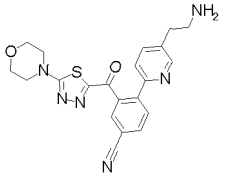
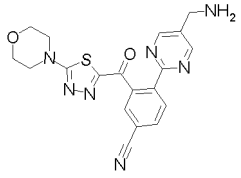
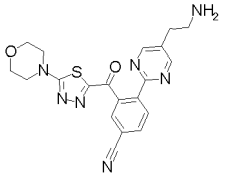
[Table 1-135]

Compound number	Structural formula	Compound name
1073		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-[2,2-difluoroethyl (ethyl)amino]-2-methylpyrazole-3-carbonyl]benzonitrile
1074		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-[2,2-difluoroethyl (ethyl)amino]-2-methylpyrazole-3-carbonyl]benzonitrile
1075		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-methyl-5-(methylamino) pyrazole-3-carbonyl]benzonitrile
1076		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(4-methyl-2-morpholin-4-yl-1,3-thiazole-5-carbonyl)benzonitrile
1077		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-morpholin-4-yl-4-(trifluoromethyl)-1,3-thiazole-5-carbonyl]benzonitrile
1078		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-morpholin-4-yl-4-(trifluoromethyl)-1,3-thiazole-5-carbonyl]benzonitrile
1079		4-[4-(2-aminoethyl)phenyl]-3-(6-morpholin-4-ylpyridazine-4-carbonyl)benzonitrile
1080		4-[5-(aminomethyl)pyridin-2-yl]-3-[2-morpholin-4-yl-4-(trifluoromethyl)-1,3-thiazole-5-carbonyl]benzonitrile

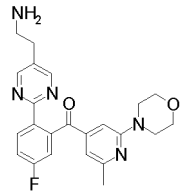
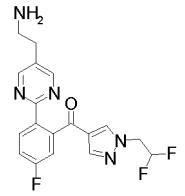
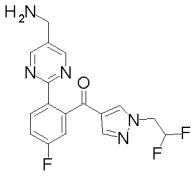
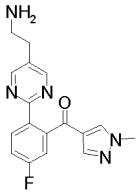
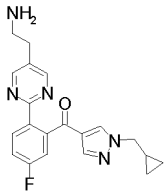
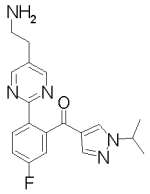
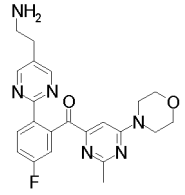
[Table 1-136]

Compound number	Structural formula	Compound name
1081		4-[4-(2-aminoethyl)phenyl]-3-(2-morpholin-4-yl-1,3-oxazole-5-carbonyl)benzonitrile
1082		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-morpholin-4-yl-1,3-oxazole-5-carbonyl)benzonitrile
1083		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-morpholin-4-yl-1,3-oxazole-5-carbonyl)benzonitrile
1084		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-morpholin-4-yl-1,3-oxazole-5-carbonyl)benzonitrile
1085		4-[5-(aminomethyl)pyridin-2-yl]-3-(2-morpholin-4-yl-1,3-oxazole-5-carbonyl)benzonitrile
1086		4-[4-(2-aminoethyl)phenyl]-3-(5-morpholin-4-yl-1,3,4-oxadiazole-2-carbonyl)benzonitrile
1087		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-morpholin-4-yl-4-(trifluoromethyl)-1,3-thiazole-5-carbonyl]benzonitrile
1088		4-[4-(2-aminoethyl)phenyl]-3-(5-morpholin-4-yl-1,3,4-thiadiazole-2-carbonyl)benzonitrile

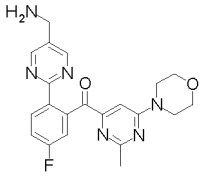
[Table 1-137]

Compound number	Structural formula	Compound name
1089		4-[5-(aminomethyl)pyridin-2-yl]-3-(5-morpholin-4-yl-1,3,4-oxadiazole-2-carbonyl)benzonitrile
1090		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(5-morpholin-4-yl-1,3,4-oxadiazole-2-carbonyl)benzonitrile
1091		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(5-morpholin-4-yl-1,3,4-oxadiazole-2-carbonyl)benzonitrile
1092		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-morpholin-4-yl-1,3,4-oxadiazole-2-carbonyl)benzonitrile
1093		4-[5-(aminomethyl)pyridin-2-yl]-3-(5-morpholin-4-yl-1,3,4-thiadiazole-2-carbonyl)benzonitrile
1094		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(5-morpholin-4-yl-1,3,4-thiadiazole-2-carbonyl)benzonitrile
1095		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(5-morpholin-4-yl-1,3,4-thiadiazole-2-carbonyl)benzonitrile
1096		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-morpholin-4-yl-1,3,4-thiadiazole-2-carbonyl)benzonitrile

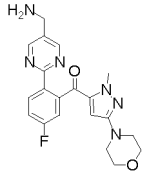
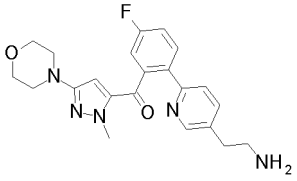
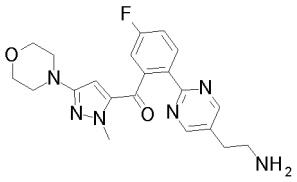
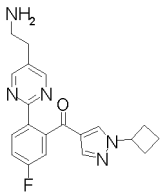
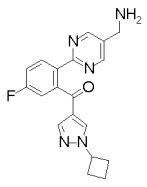
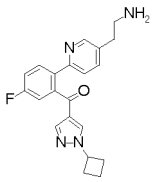
[Table 1-138]

Compound number	Structural formula	Compound name
1097		[2-[5-(2-aminoethyl)pyrimidin-2-yl]-5-fluorophenyl]-(2-methyl-6-morpholin-4-ylpyridin-4-yl)methanone
1098		[2-[5-(2-aminoethyl)pyrimidin-2-yl]-5-fluorophenyl]-[1-(2,2-difluoroethyl) pyrazol-4-yl]methanone
1099		[2-[5-(aminomethyl)pyrimidin-2-yl]-5-fluorophenyl]-[1-(2,2-difluoroethyl) pyrazol-4-yl]methanone
1100		[2-[5-(2-aminoethyl)pyrimidin-2-yl]-5-fluorophenyl]-(1-methylpyrazol-4-yl) methanone
1101		[2-[5-(2-aminoethyl)pyrimidin-2-yl]-5-fluorophenyl]-[1-(cyclopropylmethyl) pyrazol-4-yl]methanone
1102		[2-[5-(2-aminoethyl)pyrimidin-2-yl]-5-fluorophenyl]-(1-propan-2-ylpyrazol-4-yl)methanone
1103		[2-[5-(2-aminoethyl)pyrimidin-2-yl]-5-fluorophenyl]-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)methanone

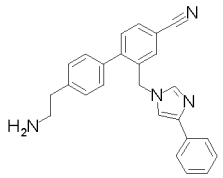
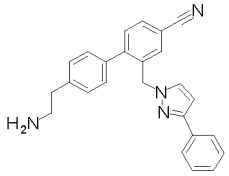
(continued)

Compound number	Structural formula	Compound name
1104		[2-[5-(aminomethyl)pyrimidin-2-yl]-5-fluorophenyl]-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)methanone

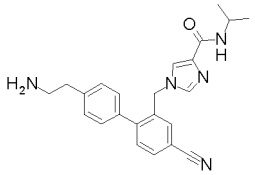
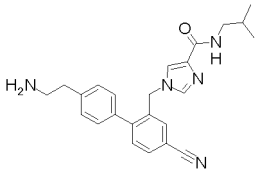
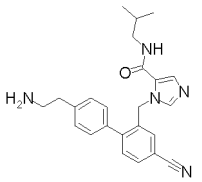
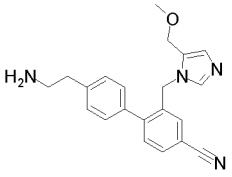
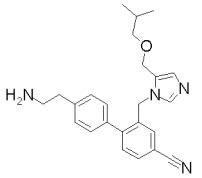
[Table 1-139]

Compound number	Structural formula	Compound name
1105		[2-[5-(aminomethyl)pyrimidin-2-yl]-5-fluorophenyl]-(2-methyl-5-morpholin-4-ylpyrazol-3-yl)methanone
1106		[2-[5-(2-aminoethyl)pyridin-2-yl]-5-fluorophenyl]-(2-methyl-5 - morpholin-4-ylpyrazol-3-yl)methanone
1107		[2-[5-(2-aminoethyl)pyrimidin-2-yl]-5-fluorophenyl]-(2-methyl-5-morpholin-4-ylpyrazol-3-yl)methanone
1108		[2-[5-(2-aminoethyl)pyrimidin-2-yl]-5-fluorophenyl]-(1-cyclobutylpyrazol-4-yl)methanone
1109		[2-[5-(aminomethyl)pyrimidin-2-yl]-5-fluorophenyl]-(1-cyclobutylpyrazol-4-yl)methanone
1110		[2-[5-(2-aminoethyl)pyridin-2-yl]-5-fluorophenyl]-(1-cyclobutylpyrazol-4-yl)methanone

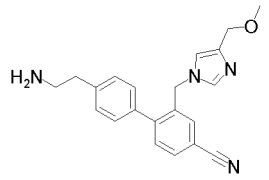
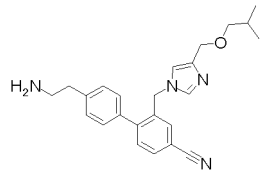
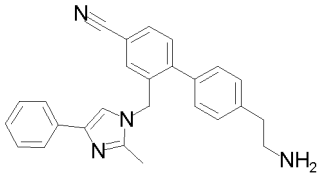
(continued)

Compound number	Structural formula	Compound name
1111		4-[4-(2-aminoethyl)phenyl]-3-[(4-phenylimidazol-1-yl) methyl]benzonitrile
1112		4-[4-(2-aminoethyl)phenyl]-3-[(3-phenylpyrazol-1-yl) methyl]benzonitrile

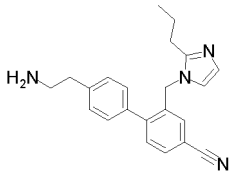
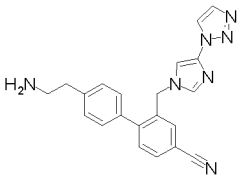
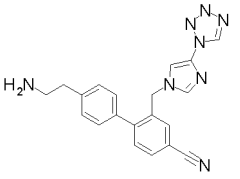
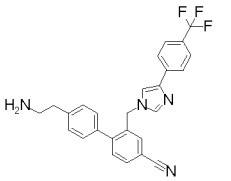
[Table 1-140]

Compound number	Structural formula	Compound name
1113		1-[[2-[4-(2-aminoethyl)phenyl]-5-cyanophenyl]methyl]-N-propan-2-ylimidazole-4-carboxamide
1114		1-[[2-[4-(2-aminoethyl)phenyl]-5-cyanophenyl]methyl]-N-(2-methylpropyl)imidazole-4-carboxamide
1115		3-[[2-[4-(2-aminoethyl)phenyl]-5-cyanophenyl]methyl]-N-(2-methylpropyl)imidazole-4-carboxamide
1116		4-[4-(2-aminoethyl)phenyl]-3-[[5-(methoxymethyl)imidazol-1-yl]methyl]benzonitrile
1117		4-[4-(2-aminoethyl)phenyl]-3-[[5-(2-methylpropoxymethyl) imidazol-1-yl]methyl]benzonitrile

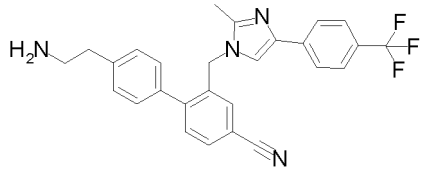
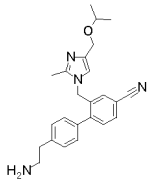
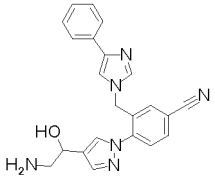
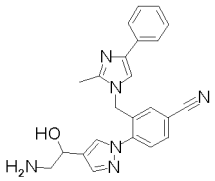
(continued)

Compound number	Structural formula	Compound name
1118		4-[4-(2-aminoethyl)phenyl]-3-[[4-(methoxymethyl)imidazol-1-yl]methyl]benzonitrile
1119		4-[4-(2-aminoethyl)phenyl]-3-[[4-(2-methylpropoxymethyl) imidazol-1-yl]methyl]benzonitrile
1120		4-[4-(2-aminoethyl)phenyl]-3-[(2-methyl-4-phenylimidazol-1-yl)methyl]benzonitrile

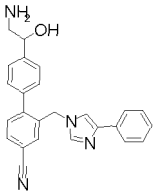
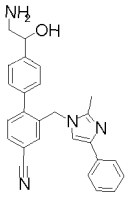
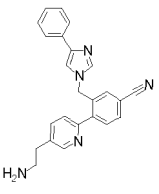
[Table 1-141]

Compound number	Structural formula	Compound name
1121		4-[4-(2-aminoethyl)phenyl]-3-[(2-propylimidazol-1-yl) methyl]benzonitrile
1122		4-[4-(2-aminoethyl)phenyl]-3-[[4-(triazol-1-yl)imidazol-1-yl]methyl]benzonitrile
1123		4-[4-(2-aminoethyl)phenyl]-3-[[4-(tetrazol-1-yl)imidazol-1- yl]methyl]benzonitrile
1124		4-[4-(2-aminoethyl)phenyl]-3-[[4-[4-(trifluoromethyl) phenyl]imidazol-1-yl]methyl]benzonitrile

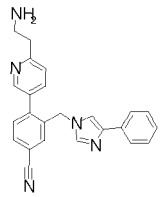
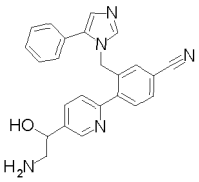
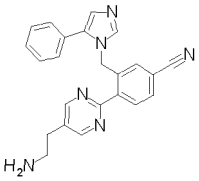
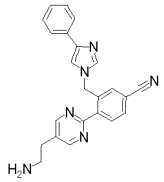
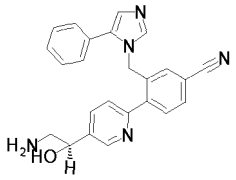
(continued)

Compound number	Structural formula	Compound name
1125		4-[4-(2-aminoethyl)phenyl]-3-[[2-methyl-4-[4-(trifluoromethyl)phenyl]imidazol-1-yl]methyl] benzonitrile
1126		4-[4-(2-aminoethyl)phenyl]-3-[[2-methyl-4-(propan-2-yloxymethyl)imidazol-1-yl]methyl]benzonitrile
1127		4-[4-(2-amino-1-hydroxyethyl)pyrazol-1-yl]-3-[(4-phenylimidazol-1-yl)methyl]benzonitrile
1128		4-[4-(2-amino-1-hydroxyethyl)pyrazol-1-yl]-3-[(2-methyl-4-phenylimidazol-1-yl)methyl]benzonitrile

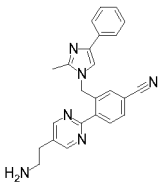
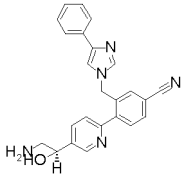
[Table 1-142]

Compound number	Structural formula	Compound name
1129		4-[4-(2-amino-1-hydroxyethyl)phenyl]-3-[(4-phenylimidazol-1-yl) methyl]benzonitrile
1130		4-[4-(2-amino-1-hydroxyethyl)phenyl]-3-[(2-methyl-4-phenylimidazol-1-yl)methyl]benzonitrile
1131		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[(4-phenylimidazol-1-yl)methyl] benzonitrile

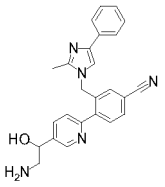
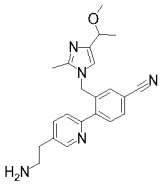
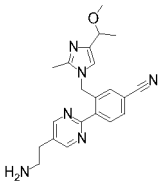
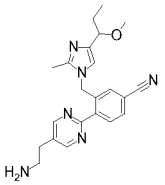
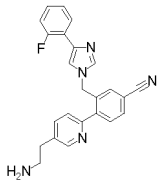
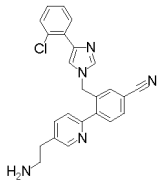
(continued)

Compound number	Structural formula	Compound name
1132		4-[6-(2-aminoethyl)pyridin-3-yl]-3-[(4-phenylimidazol-1-yl)methyl] benzonitrile
1133		4-[5-(2-amino-1-hydroxyethyl)pyridin-2-yl]-3-[(5-phenylimidazol-1-yl)methyl]benzonitrile
1134		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(5-phenylimidazol-1-yl) methyl]benzonitrile
1135		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(4-phenylimidazol-1-yl) methyl]benzonitrile
1136		4-[5-[(1R)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[(5-phenylimidazol-1-yl)methyl]benzonitrile

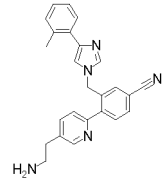
[Table 1-143]

Compound number	Structural formula	Compound name
1137		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(2-methyl-4-phenylimidazol-1-yl) methyl]benzonitrile
1138		4-[5-[(1R)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[(4-phenylimidazol-1-yl)methyl]benzonitrile

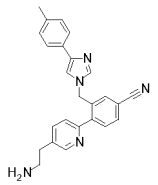
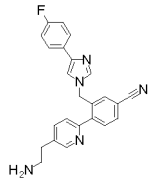
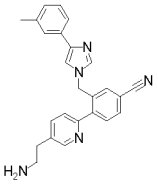
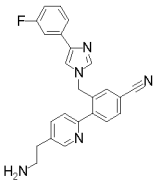
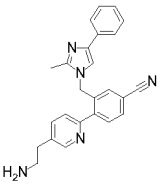
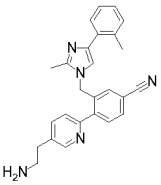
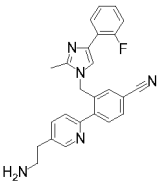
(continued)

Compound number	Structural formula	Compound name
1139		4-[5-(2-amino-1-hydroxyethyl)pyridin-2-yl]-3-[(2-methyl-4-phenylimidazol-1-yl)methyl]benzonitrile
1140		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[[4-(1-methoxyethyl)-2-methylimidazol-1-yl]methyl]benzonitrile
1141		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[[4-(1-methoxyethyl)-2-methylimidazol-1-yl]methyl]benzonitrile
1142		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[[4-(1-methoxypropyl)-2-methylimidazol-1-yl]methyl]benzonitrile
1143		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[[4-(2-fluorophenyl)imidazol-1-yl]methyl]benzonitrile
1144		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[[4-(2-chlorophenyl)imidazol-1-yl]methyl]benzonitrile

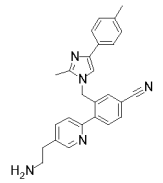
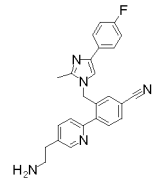
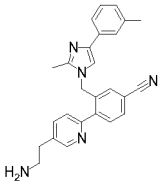
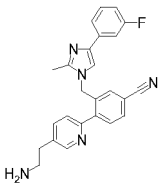
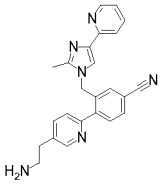
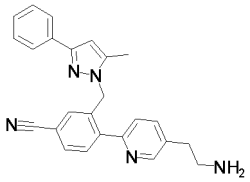
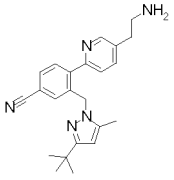
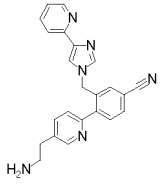
[Table 1-144]

Compound number	Structural formula	Compound name
1145		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[[4-(2-methylphenyl)imidazol-1-yl]methyl]benzonitrile

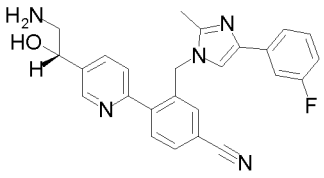
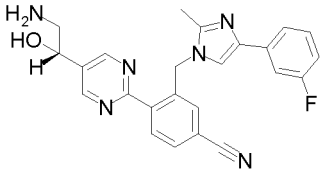
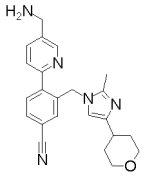
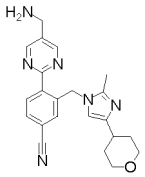
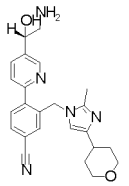
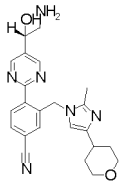
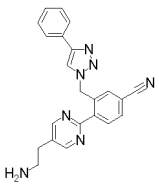
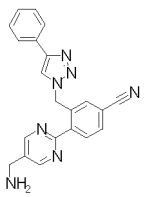
(continued)

Compound number	Structural formula	Compound name
1146		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[[4-(4-methylphenyl)imidazol-1-yl] methyl]benzonitrile
1147		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[[4-(4-fluorophenyl)imidazol-1-yl] methyl]benzonitrile
1148		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[[4-(3-methylphenyl)imidazol-1-yl] methyl]benzonitrile
1149		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[[4-(3-fluorophenyl)imidazol-1-yl] methyl]benzonitrile
1150		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[(2-methyl-4-phenylimidazol-1-yl) methyl]benzonitrile
1151		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[[2-methyl-4-(2-methylphenyl) imidazol-1-yl]methyl]benzonitrile
1152		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[[4-(2-fluorophenyl)-2-methylimidazol-1-yl]methyl]benzonitrile

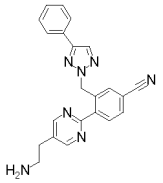
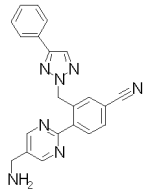
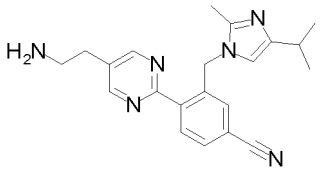
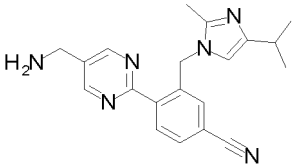
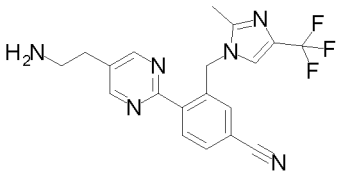
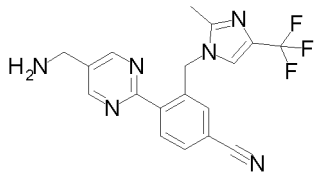
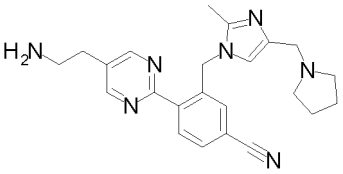
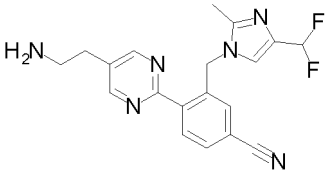
[Table 1-145]

Compound number	Structural formula	Compound name
1153		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[[2-methyl-4-(4-methylphenyl) imidazol-1-yl]methyl]benzonitrile
1154		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[[4-(4-fluorophenyl)-2-methylimidazol-1-yl]methyl]benzonitrile
1155		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[[2-methyl-4-(3-methylphenyl) imidazol-1-yl]methyl]benzonitrile
1156		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[[4-(3-fluorophenyl)-2-methylimidazol-1-yl]methyl]benzonitrile
1157		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[(2-methyl-4-pyridin-2-ylimidazol-1-yl)methyl]benzonitrile
1158		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[(5-methyl-3-phenylpyrazol-1-yl)methyl]benzonitrile
1159		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[(3-tert-butyl-5-methylpyrazol-1-yl)methyl]benzonitrile
1160		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[(4-pyridin-2-ylimidazol-1-yl) methyl]benzonitrile

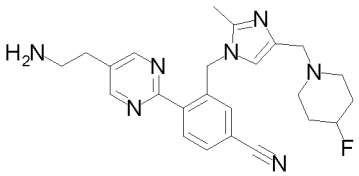
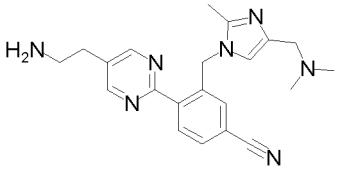
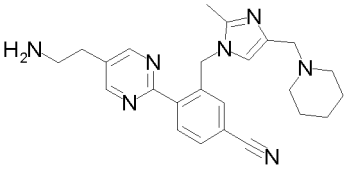
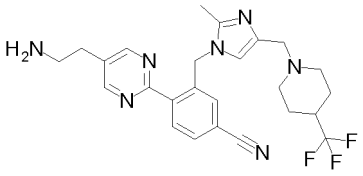
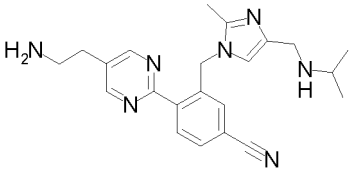
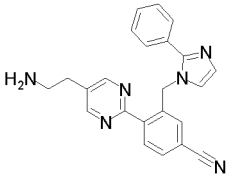
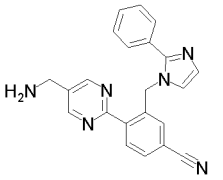
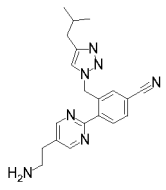
[Table 1-146]

Compound number	Structural formula	Compound name
1161		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[[4-(3-fluorophenyl)-2-methylimidazol-1-yl]methyl]benzonitrile
1162		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyrimidin-2-yl]-3-[[4-(3-fluorophenyl)-2-methylimidazol-1-yl]methyl]benzonitrile
1163		4-[5-(aminomethyl)pyridin-2-yl]-3-[[2-methyl-4-(oxan-4-yl)imidazol-1-yl]methyl]benzonitrile
1164		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[[2-methyl-4-(oxan-4-yl)imidazol-1-yl]methyl]benzonitrile
1165		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyridin-2-yl]-3-[[2-methyl-4-(oxan-4-yl)imidazol-1-yl]methyl]]benzonitrile
1166		4-[5-[(1S)-2-amino-1-hydroxyethyl]pyrimidin-2-yl]-3-[[2-methyl-4-(oxan-4-yl)imidazol-1-yl]methyl]]benzonitrile
1167		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(4-phenyltriazol-1-yl)methyl]benzonitrile
1168		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[(4-phenyltriazol-1-yl)methyl]benzonitrile

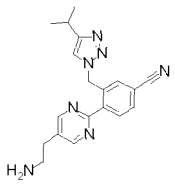
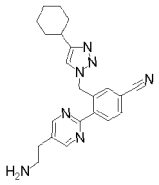
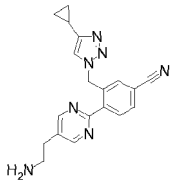
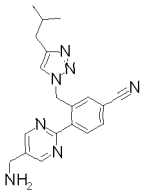
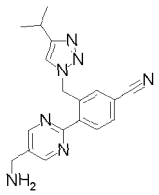
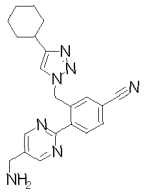
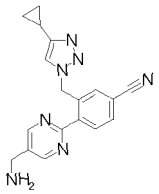
[Table 1-147]

Compound number	Structural formula	Compound name
1169		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(4-phenyltriazol-2-yl) methyl]benzonitrile
1170		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[(4-phenyltriazol-2-yl) methyl]benzonitrile
1171		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(2-methyl-4-propan-2-ylimidazol-1-yl)methyl]benzonitrile
1172		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[(2-methyl-4-propan-2-ylimidazol-1-yl)methyl]benzonitrile
1173		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[[2-methyl-4-(trifluoromethyl)imidazol-1-yl]methyl]benzonitrile
1174		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[[2-methyl-4-(trifluoromethyl)imidazol-1-yl]methyl]benzonitrile
1175		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[[2-methyl-4-(pyrrolidin-1-ylmethyl)imidazol-1-yl]methyl]benzonitrile
1176		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[[4-(difluoromethyl)-2-methylimidazol-1-yl]methyl]benzonitrile

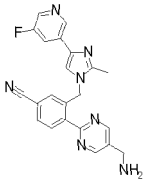
[Table 1-148]

Compound number	Structural formula	Compound name
1177		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[[4-[(4-fluoropiperidin-1-yl)methyl]-2-methylimidazol-1-yl]methyl]benzonitrile
1178		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[[4-[(dimethylamino)methyl]-2-methylimidazol-1-yl]methyl]benzonitrile
1179		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[[2-methyl-4-(piperidin-1-ylmethyl)imidazol-1-yl]methyl]benzonitrile
1180		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[[2-methyl-4-[[4-(trifluoromethyl)piperidin-1-yl]methyl]imidazol-1-yl]methyl]benzonitrile
1181		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[[2-methyl-4-[(propan-2-ylamino)methyl]imidazol-1-yl]methyl]benzonitrile
1182		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(2-phenylimidazol-1-yl)methyl]benzonitrile
1183		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[(2-phenylimidazol-1-yl)methyl]benzonitrile
1184		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[[4-(2-methylpropyl)triazol-1-yl]methyl]benzonitrile

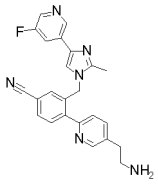
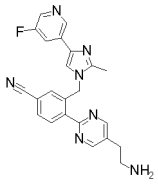
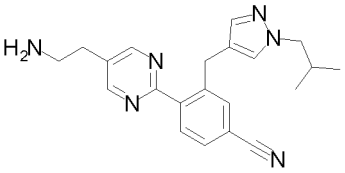
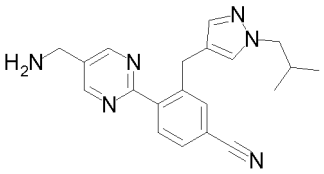
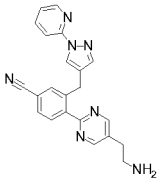
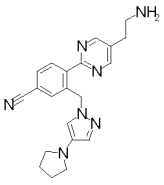
[Table 1-149]

Compound number	Structural formula	Compound name
1185		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(4-prop an-2-yltriazol-1-yl)methyl] benzonitrile
1186		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(4-cyclohexyltriazol-1-yl)methyl] benzonitrile
1187		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(4-cyclopropyltriazol-1-yl)methyl] benzonitrile
1188		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[[4-(2-methylpropyl)triazol-1-yl] methyl]benzonitrile
1189		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[(4-propan-2-yltriazol-1 - yl)methyl] benzonitrile
1190		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[(4-cyclohexyltriazol-1-yl)methyl] benzonitrile
1191		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[(4-cyclopropyltriazol-1-yl)methyl] benzonitrile

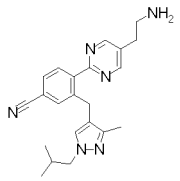
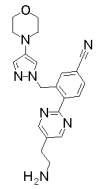
(continued)

Compound number	Structural formula	Compound name
1192		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[[4-(5-fluoropyridin-3-yl)-2-methylimidazol-1-yl]methyl]benzonitrile

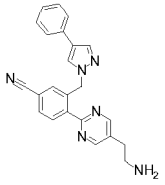
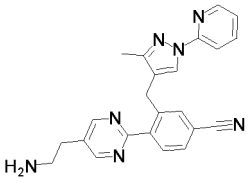
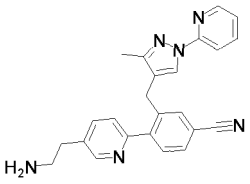
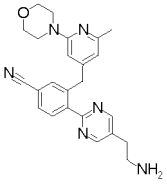
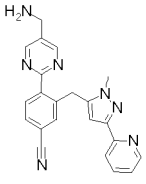
[Table 1-150]

Compound number	Structural formula	Compound name
1193		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[[4-(5-fluoropyridin-3-yl)-2-methylimidazol-1-yl]methyl]benzonitrile
1194		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[[4-(5-fluoropyridin-3-yl)-2-methylimidazol-1-yl]methyl] benzonitrile
1195		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[[1-(2-methylpropyl)pyrazol-4-yl]methyl]benzonitrile
1196		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[[1-(2-methylpropyl)pyrazol-4-yl]methyl]benzonitrile
1197		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(1-pyridin-2-ylpyrazol-4-yl)methyl]benzonitrile
1198		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(4-pyrrolidin-1-ylpyrazol-1-yl)methyl]benzonitrile

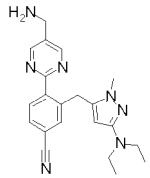
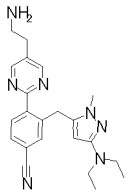
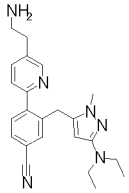
(continued)

Compound number	Structural formula	Compound name
1199		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[[3-methyl-1-(2-methylpropyl)pyrazol-4-yl]methyl]benzonitrile
1200		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(4-morpholin-4-ylpyrazol-1-yl)methyl]benzonitrile

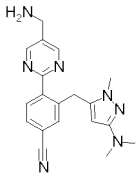
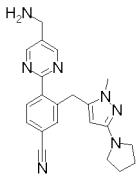
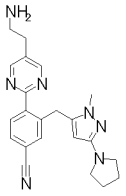
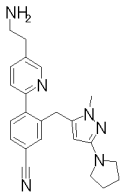
[Table 1-151]

Compound number	Structural formula	Compound name
1201		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(4-phenylpyrazol-1-yl) methyl]benzonitrile
1202		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(3-methyl-1-pyridin-2-ylpyrazol-4-yl)methyl]benzonitrile
1203		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[(3-methyl-1-pyridin-2-ylpyrazol-4-yl)methyl]benzonitrile
1204		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(2-methyl-6-morpholin-4-ylpyridin-4-yl)methyl]benzonitrile
1205		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[(2-methyl-5-pyridin-2-ylpyrazol-3-yl)methyl]benzonitrile

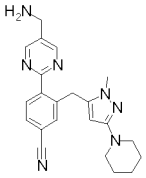
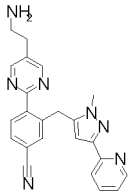
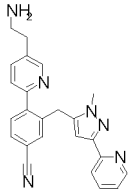
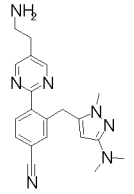
(continued)

Compound number	Structural formula	Compound name
1206		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[[5-(diethylamino)-2-methylpyrazol-3-yl]methyl]benzonitrile
1207		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[[5-(diethylamino)-2-methylpyrazol-3-yl]methyl]benzonitrile
1208		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[[5-(diethylamino)-2-methylpyrazol-3-yl]methyl]benzonitrile

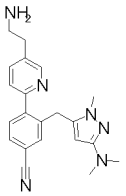
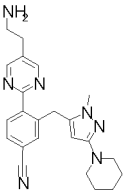
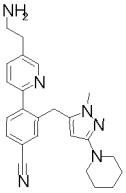
[Table 1-152]

Compound number	Structural formula	Compound name
1209		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[[5-(dimethylamino)-2-methylpyrazol-3-yl]methyl]benzonitrile
1210		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[(2-methyl-5-pyrrolidin-1-ylpyrazol-3-yl)methyl]benzonitrile
1211		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(2-methyl-5-pyrrolidin-1-ylpyrazol-3-yl)methyl]benzonitrile
1212		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[(2-methyl-5-pyrrolidin-1-ylpyrazol-3-yl)methyl]benzonitrile

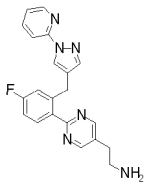
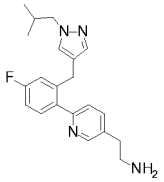
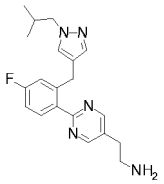
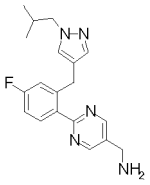
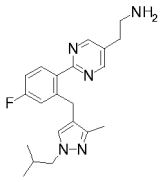
(continued)

Compound number	Structural formula	Compound name
1213		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[(2-methyl-5-piperidin-1-ylpyrazol-3-yl)methyl]benzonitrile
1214		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(2-methyl-5-pyridin-2-ylpyrazol-3-yl)methyl]benzonitrile
1215		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[(2-methyl-5-pyridin-2-ylpyrazol-3-yl)methyl]benzonitrile
1216		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[[5-(dimethylamino)-2-methylpyrazol-3-yl]methyl]benzonitrile

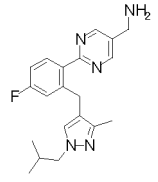
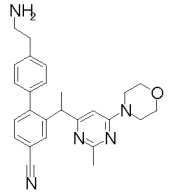
[Table 1-153]

Compound number	Structural formula	Compound name
1217		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[[5-(dimethylamino)-2-methylpyrazol-3-yl]methyl]benzonitrile
1218		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(2-methyl-5-piperidin-1-ylpyrazol-3-yl)methyl]benzonitrile
1219		4-[5-(2-aminoethyl)pyridin-2-yl]-3-[(2-methyl-5-piperidin-1-ylpyrazol-3-yl)methyl]benzonitrile

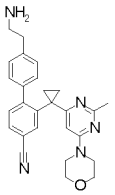
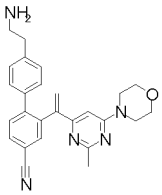
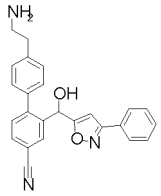
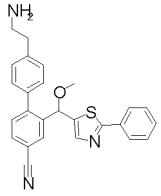
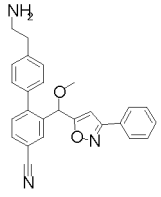
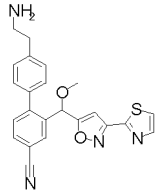
(continued)

Compound number	Structural formula	Compound name
1220		2-[2-[4-fluoro-2-[(1-pyridin-2-ylpyrazol-4-yl)methyl]phenyl]pyrimidin-5-yl]ethanamine
1221		2-[6-[4-fluoro-2-[[1-(2-methylpropyl)pyrazol-4-yl]methyl]phenyl] pyridin-3- yl]ethanamine
1222		2-[2-[4-fluoro-2-[[1-(2-methylpropyl)pyrazol-4-yl]methyl]phenyl] pyrimidin-5-yl]ethanamine
1223		[2-[4-fluoro-2-[[1-(2-methylpropyl)pyrazol-4-yl]methyl]phenyl] pyrimidin-5-yl]methanamine
1224		2-[2-[4-fluoro-2-[[3-methyl-1-(2-methylpropyl)pyrazol-4-yl]methyl] phenyl]pyrimidin-5-yl]ethanamine

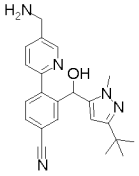
[Table 1-154]

Compound number	Structural formula	Compound name
1225		[2-[4-fluoro-2-[[3-methyl-1-(2-methylpropyl)pyrazol-4-yl]methyl] phenyl]pyrimidin-5-yl]methanamine
1226		4-[4-(2-aminoethyl)phenyl]-3-[1-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)ethyl]benzonitrile

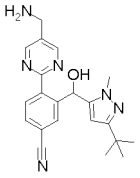
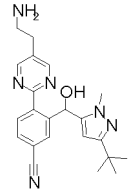
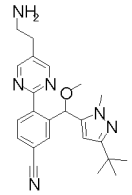
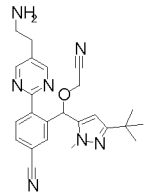
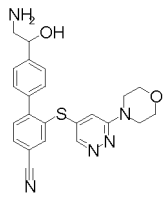
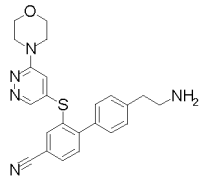
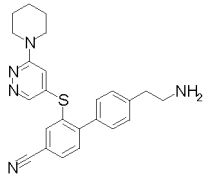
(continued)

Compound number	Structural formula	Compound name
1227		4-[4-(2-aminoethyl)phenyl]-3-[1-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)cyclopropyl]benzonitrile
1228		4-[4-(2-aminoethyl)phenyl]-3-[1-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)ethenyl]benzonitrile
1229		4-[4-(2-aminoethyl)phenyl]-3-[hydroxy-(3-phenyl-1,2-oxazol-5-yl) methyl]benzonitrile
1230		4-[4-(2-aminoethyl)phenyl]-3-[methoxy-(2-phenyl-1,3-thiazol-5-yl) methyl]benzonitrile
1231		4-[4-(2-aminoethyl)phenyl]-3-[methoxy-(3-phenyl-1,2-oxazol-5-yl) methyl]benzonitrile
1232		4-[4-(2-aminoethyl)phenyl]-3-[methoxy-[3-(1,3-thiazol-2-yl)-1,2-oxazol-5-yl]methyl]benzonitrile

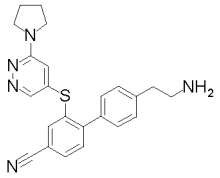
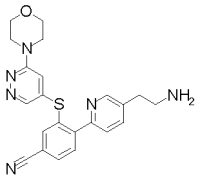
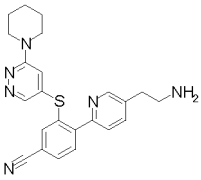
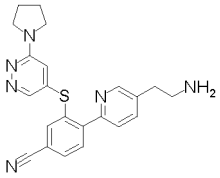
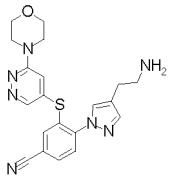
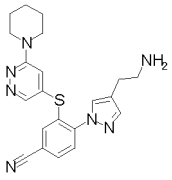
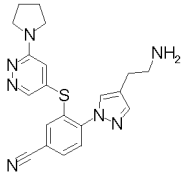
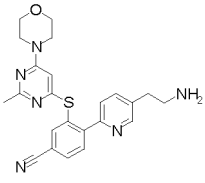
[Table 1-155]

Compound number	Structural formula	Compound name
1233		4-[5-(aminomethyl)pyridin-2-yl]-3-[(5-tert-butyl-2-methylpyrazol-3-yl)-hydroxymethyl]benzonitrile

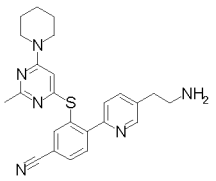
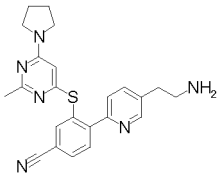
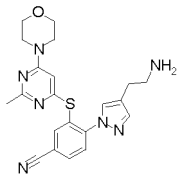
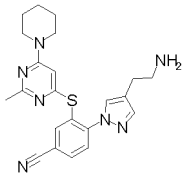
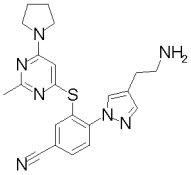
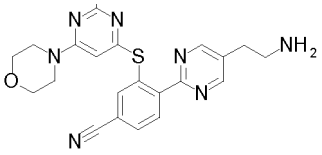
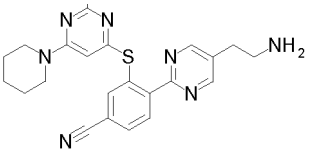
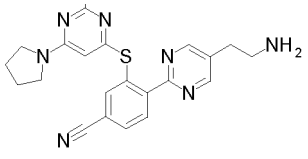
(continued)

Compound number	Structural formula	Compound name
1234		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[(5-tert-butyl-2-methylpyrazol-3-yl)-hydroxymethyl]benzonitrile
123 5		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(5-tert-butyl-2-methylpyrazol-3-yl)-hydroxymethyl]benzonitrile
1236		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(5-tert-butyl-2-methylpyrazol-3-yl)-methoxymethyl]benzonitrile
1237		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(5-tert-butyl-2-methylpyrazol-3-yl)-(cyanomethoxy)methyl]benzonitrile
1238		4-[4-(2-amino-1-hydroxyethyl)phenyl]-3-(6-morpholin-4-ylpyridazin-4-yl)sulfanylbenzonitrile
1239		4-[4-(2-aminoethyl)phenyl]-3-(6-morpholin-4-ylpyridazin-4-yl) sulfanylbenzonitrile
1240		4-[4-(2-aminoethyl)phenyl]-3-(6-piperidin-1 -ylpyridazin-4-yl) sulfanylbenzonitrile

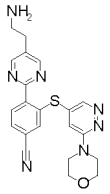
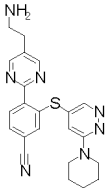
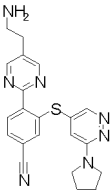
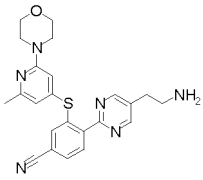
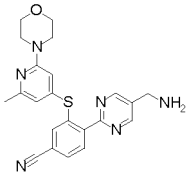
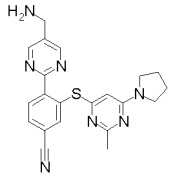
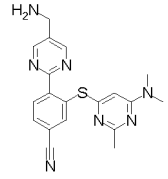
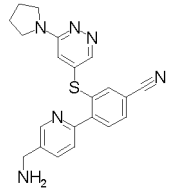
[Table 1-156]

Compound number	Structural formula	Compound name
1241		4-[4-(2-aminoethyl)phenyl]-3-(6-pyrrolidin-1-ylpyridazin-4-yl) sulfanylbenzonitrile
1242		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(6-morpholin-4-ylpyridazin-4-yl) sulfanylbenzonitrile
1243		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(6-piperidin-1-ylpyridazin-4-yl) sulfanylbenzonitrile
1244		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(6-pyrrolidin-1-ylpyridazin-4-yl) sulfanylbenzonitrile
1245		4-[4-(2-aminoethyl)pyrazol-1-yl]-3-(6-morpholin-4-ylpyridazin-4-yl) sulfanylbenzonitrile
1246		4-[4-(2-aminoethyl)pyrazol-1-yl]-3-(6-piperidin-1-ylpyridazin-4-yl) sulfanylbenzonitrile
1247		4-[4-(2-aminoethyl)pyrazol-1-yl]-3-(6-pyrrolidin-1-ylpyridazin-4-yl) sulfanylbenzonitrile
1248		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)sulfanylbenzonitrile

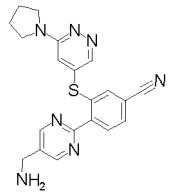
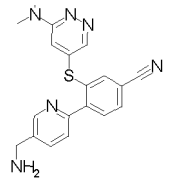
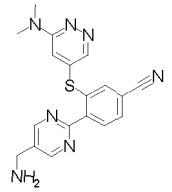
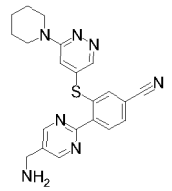
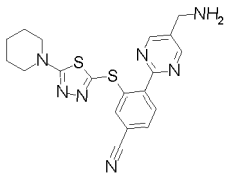
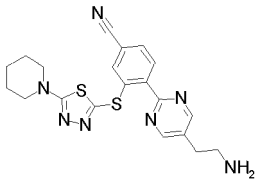
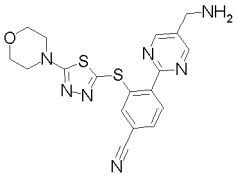
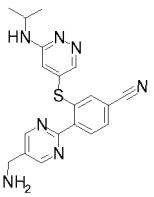
[Table 1-157]

Compound number	Structural formula	Compound name
1249		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-6-piperidin-1-ylpyrimidin-4-yl)sulfanylbenzonitrile
1250		4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-6-pyrrolidin-1-ylpyrimidin-4-yl)sulfanylbenzonitrile
1251		4-[4-(2-aminoethyl)pyrazol-1-yl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)sulfanylbenzonitrile
1252		4-[4-(2-aminoethyl)pyrazol-1-yl]-3-(2-methyl-6-piperidin-1-ylpyrimidin-4-yl)sulfanylbenzonitrile
1253		4-[4-(2-aminoethyl)pyrazol-1-yl]-3-(2-methyl-6-pyrrolidin-1-ylpyrimidin-4-yl)sulfanylbenzonitrile
1254		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)sulfanylbenzonitrile
1255		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-piperidin-1-ylpyrimidin-4-yl)sulfanylbenzonitrile
1256		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-pyrrolidin-1-ylpyrimidin-4-yl)sulfanylbenzonitrile

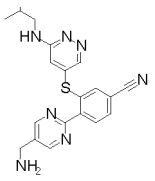
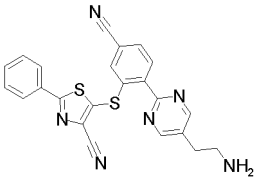
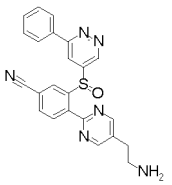
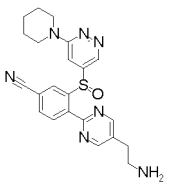
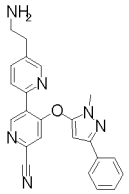
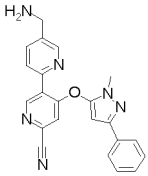
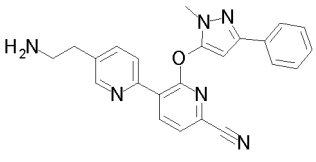
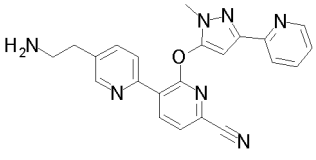
[Table 1-158]

Compound number	Structural formula	Compound name
1257		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(6-morpholin-4-ylpyridazin-4-yl) sulfanylbenzonitrile
1258		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(6-piperidin-1-ylpyridazin-4-yl) sulfanylbenzonitrile
1259		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(6-pyrrolidin-1-ylpyridazin-4-yl) sulfanylbenzonitrile
1260		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)sulfanylbenzonitrile
1261		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)sulfanylbenzonitrile
1262		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-6-pyrrolidin-1-ylpyrimidin-4-yl)sulfanylbenzonitrile
1263		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(dimethylamino)-2-methylpyrimidin-4-yl] sulfanylbenzonitrile
1264		4-[5-(aminomethyl)pyridin-2-yl]-3-(6-pyrrolidin-1-ylpyridazin-4-yl) sulfanylbenzonitrile

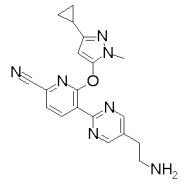
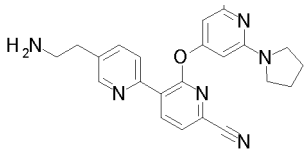
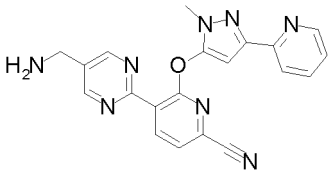
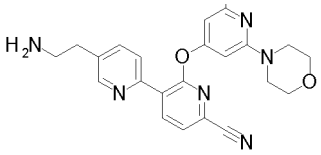
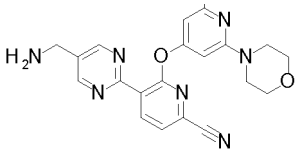
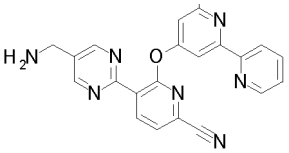
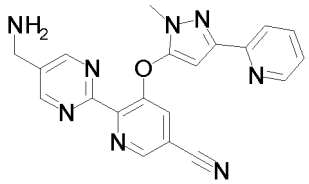
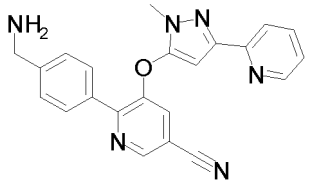
[Table 1-159]

Compound number	Structural formula	Compound name
1265		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(6-pyrrolidin-1-ylpyridazin-4-yl)sulfanylbenzonitrile
1266		4-[5-(aminomethyl)pyridin-2-yl]-3-[6-(dimethylamino)pyridazin-4-yl]sulfanylbenzonitrile
1267		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(dimethylamino) pyridazin-4-yl] sulfanylbenzonitrile
1268		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(6-piperidin-1-ylpyridazin-4-yl)sulfanylbenzonitrile
1269		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[(5-piperidin-1-yl-1,3,4-thiadiazol-2-yl)sulfanyl]benzonitrile
1270		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(5-piperidin-1-yl-1,3,4-thiadiazol-2-yl)sulfanyl]benzonitrile
1271		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[(5-morpholin-4-yl-1,3,4-thiadiazol-2-yl)sulfanyl]benzonitrile
1272		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(propan-2-ylamino) pyridazin-4-yl] sulfanylbenzonitrile

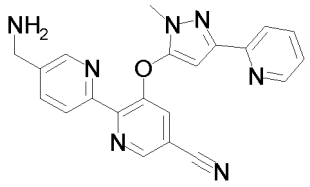
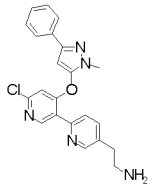
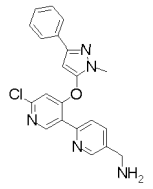
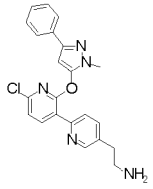
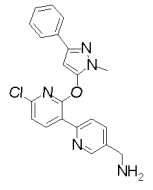
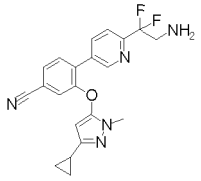
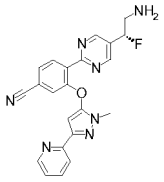
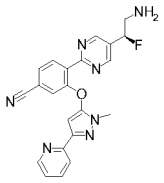
[Table 1-160]

Compound number	Structural formula	Compound name
1273		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(2-methylpropylamino)pyridazin-4-yl] sulfanylbenzonitrile
1274		5-[2-[5-(2-aminoethyl)pyrimidin-2-yl]-5-cyanophenyl] sulfanyl-2-phenyl-1,3-thiazole-4-carbonitrile
1275		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(6-phenylpyridazin-4-yl)sulfinylbenzonitrile
1276		4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(6-piperidin-1-ylpyridazin-4-yl)sulfinylbenzonitrile
1277		5-[5-(2-aminoethyl)pyridin-2-yl]-4-(2-methyl-5-phenylpyrazol-3-yl)oxypyridine-2-carbonitrile
1278		5-[5-(aminomethyl)pyridin-2-yl]-4-(2-methyl-5-phenylpyrazol-3-yl)oxypyridine-2-carbonitrile
1279		5-[5-(2-aminoethyl)pyridin-2-yl]-6-(2-methyl-5-phenylpyrazol-3-yl)oxypyridine-2-carbonitrile
1280		5-[5-(2-aminoethyl)pyridin-2-yl]-6-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxypyridine-2-carbonitrile

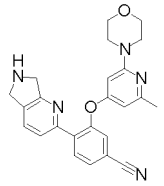
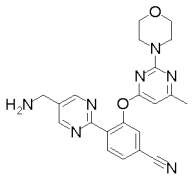
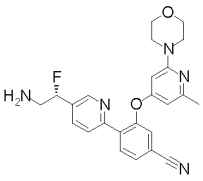
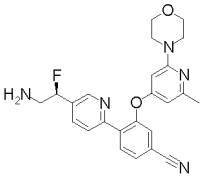
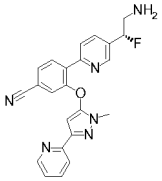
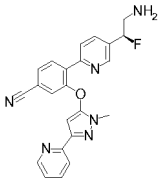
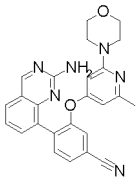
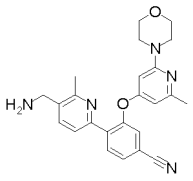
[Table 1-161]

Compound number	Structural formula	Compound name
1281		5-[5-(2-aminoethyl)pyrimidin-2-yl]-6-(5-cyclopropyl-2-methylpyrazol-3 - yl)oxypyridine-2-carbonitrile
1282		5-[5-(2-aminoethyl)pyridin-2-yl]-6-(2-methyl-6-pyrrolidin-1-ylpyridin-4-yl)oxypyridine-2-carbonitrile
1283		5-[5-(aminomethyl)pyrimidin-2-yl]-6-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxypyridine-2-carbonitrile
1284		5-[5-(2-aminoethyl)pyridin-2-yl]-6-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxypyridine-2-carbonitrile
1285		5-[5-(aminomethyl)pyrimidin-2-yl]-6-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxypyridine-2-carbonitrile
1286		5-[5-(aminomethyl)pyrimidin-2-yl]-6-(2-methyl-6-pyridin-2-ylpyridin-4-yl)oxypyridine-2-carbonitrile
1287		6-[5-(aminomethyl)pyrimidin-2-yl]-5-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxypyridine-3 -carbonitrile
1288		6-[4-(aminomethyl)phenyl]-5-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxypyridine-3-carbonitrile

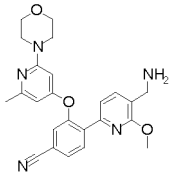
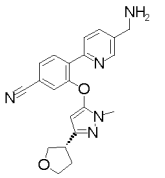
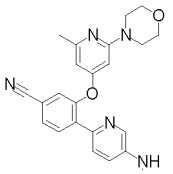
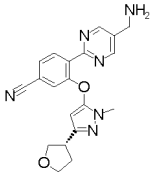
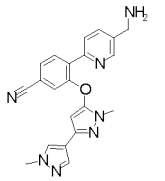
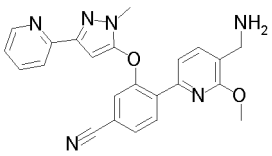
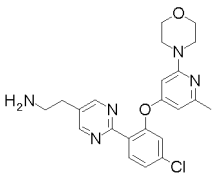
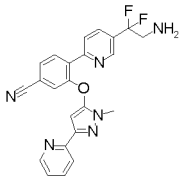
[Table 1-162]

Compound number	Structural formula	Compound name
1289		6-[5-(aminomethyl)pyridin-2-yl]-5-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxypyridine-3-carbonitrile
1290		2-[6-[6-chloro-4-(2-methyl-5-phenylpyrazol-3-yl) oxypyridin-3- yl]pyridin-3-yl]ethanamine
1291		[6-[6-chloro-4-(2-methyl-5-phenylpyrazol-3-yl)oxypyridin-3- yl]pyridin-3-yl]methanamine
1292		2-[6-[6-chloro-2-(2-methyl-5-phenylpyrazol-3-yl) oxypyridin-3- yl]pyridin-3-yl]ethanamine
1293		[6-[6-chloro-2-(2-methyl-5-phenylpyrazol-3-yl)oxypyridin-3- yl]pyridin-3-yl]methanamine
1294		4-[6-(2-amino-1,1-difluoroethyl)pyridin-3-yl]-3-(5-cyclopropyl-2-methylpyrazol-3- yl)oxybenzonitrile
1295		4-[5-[(1R)-2-amino-1-fluoroethyl]pyrimidin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
1296		4-[5-[(1S)-2-amino-1-fluoroethyl]pyrimidin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile

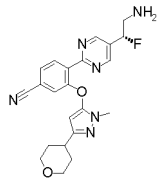
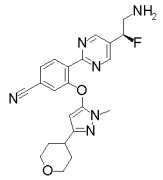
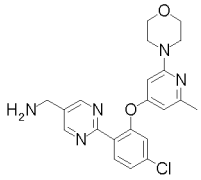
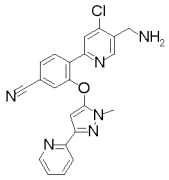
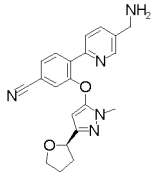
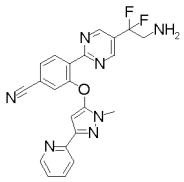
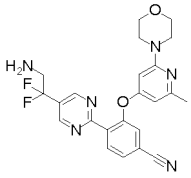
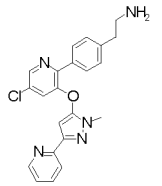
[Table 1-163]

Compound number	Structural formula	Compound name
1297		4-(6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-2-yl)-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
1298		4-[5-(aminomethyl)pyrimidin-2-yl]-3-(6-methyl-2-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
1299		4-[5-[(1R)-2-amino-1-fluoroethyl]pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
1300		4-[5-[(1S)-2-amino-1-fluoroethyl]pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
1301		4-[5-[(1R)-2-amino-1-fluoroethyl]pyridin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
1302		4-[5-[(1S)-2-amino-1-fluoroethyl]pyridin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
1303		4-(2-aminoquinazolin-8-yl)-3 -(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
1304		4-[5-(aminomethyl)-6-methylpyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile

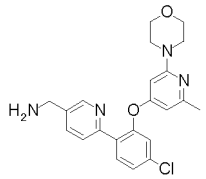
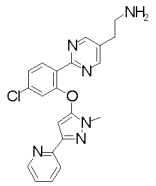
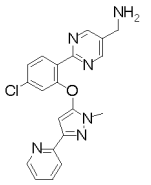
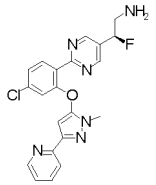
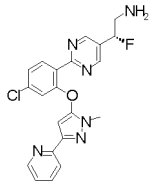
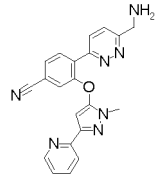
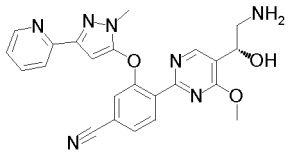
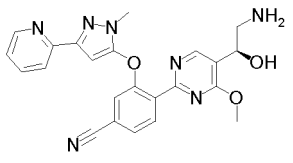
[Table 1-164]

Compound number	Structural formula	Compound name
1305		4-[5-(aminomethyl)-6-methoxypyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
1306		4-[5-(aminomethyl)pyridin-2-yl]-3-[2-methyl-5-[(3S)-oxolan-3-yl]pyrazol-3-yl]oxybenzonitrile
1307		4-[5-(methylamino)pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
1308		4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-[(3S)-oxolan-3-yl]pyrazol-3-yl]oxybenzonitrile
1309		4-[5-(aminomethyl)pyridin-2-yl]-3-[2-methyl-5-(1-methylpyrazol-4-yl)pyrazol-3-yl]oxybenzonitrile
1310		4-[5-(aminomethyl)-6-methoxypyridin-2-yl]-3 -(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
1311		2-[2-[4-chloro-2-(2-methyl-6-morpholin-4-ylpyridin-4-yl) oxyphenyl]pyrimidin-5-yl]ethanamine
1312		4-[5-(2-amino-1,1-difluoroethyl)pyridin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile

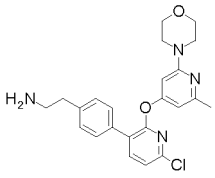
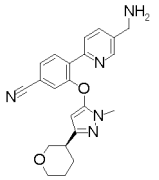
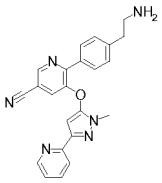
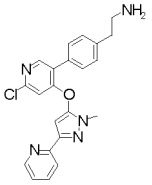
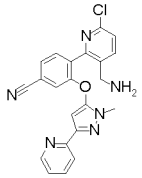
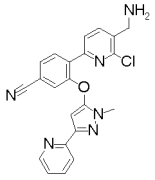
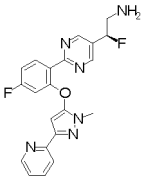
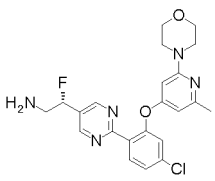
[Table 1-165]

Compound number	Structural formula	Compound name
1313		4-[5-[(1R)-2-amino-1-fluoroethyl]pyrimidin-2-yl]-3-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl]oxybenzonitrile
1314		4-[5-[(1S)-2-amino-1-fluoroethyl]pyrimidin-2-yl]-3-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl]oxybenzonitrile
1315		[2-[4-chloro-2-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxyphenyl] pyrimidin-5-yl]methanamine
1316		4-[5-(aminomethyl)-4-chloropyridin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
1317		4-[5-(aminomethyl)pyridin-2-yl]-3-[2-methyl-5-[(2R)-oxolan-2-yl] pyrazol-3-yl]oxybenzonitrile
1318		4-[5-(2-amino-1,1-difluoroethyl)pyrimidin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
1319		4-[5-(2-amino-1,1-difluoroethyl)pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
1320		2-[4-[5-chloro-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxypyridin-2-yl] phenyl]ethanamine

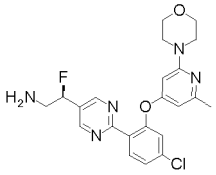
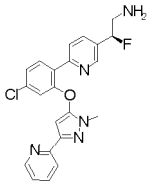
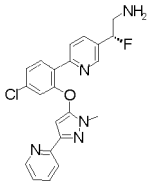
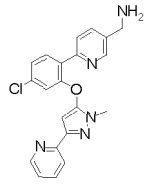
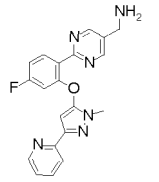
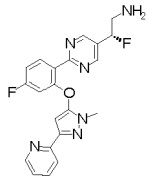
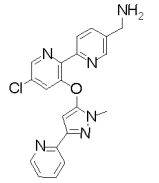
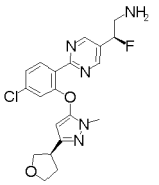
[Table 1-166]

Compound number	Structural formula	Compound name
1321		[6-[4-chloro-2-(2-methyl-6-morpholin-4-ylpyridin-4-yl) oxyphenyl]pyridin-3- yl]methanamine
1322		2-[2-[4-chloro-2-(2-methyl-5-pyridin-2-ylpyrazol-3-yl) oxyphenyl]pyrimidin-5-yl]ethanamine
1323		[2-[4-chloro-2-(2-methyl-5-pyridin-2-ylpyrazol-3-yl) oxyphenyl]pyrimidin-5-yl]methanamine
1324		(2S)-2-[2-[4-chloro-2-(2-methyl-5-pyridin-2-ylpyrazol-3-yl) oxyphenyl]pyrimidin-5-yl]-2-fluoroethanamine
1325		(2R)-2-[2-[4-chloro-2-(2-methyl-5-pyridin-2-ylpyrazol-3-yl) oxyphenyl]pyrimidin-5-yl]-2-fluoroethanamine
1326		4-[6-(aminomethyl)pyridazin-3-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
1327		4-[5-[(1R)-2-amino-1-hydroxyethyl]-4-methoxypyrimidin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
1328		4-[5-[(1S)-2-amino-1-hydroxyethyl]-4-methoxypyrimidin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile

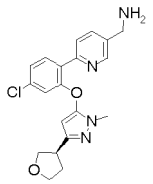
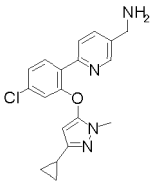
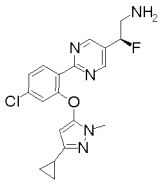
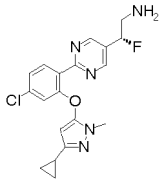
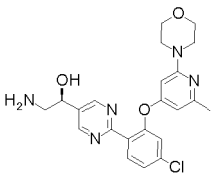
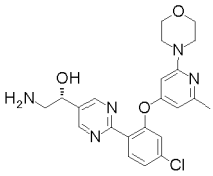
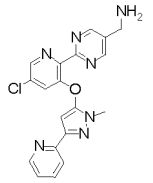
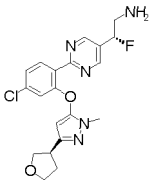
[Table 1-167]

Compound number	Structural formula	Compound name
1329		2-[4-[6-chloro-2-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxypyridin-3-yl]phenyl]ethanamine
1330		4-[5-(aminomethyl)pyridin-2-yl]-3-[2-methyl-5-[(3R)-oxan-3-yl]pyrazol-3-yl]oxybenzonitrile
1331		6-[4-(2-aminoethyl)phenyl]-5-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxypyridine-3-carbonitrile
1332		2-[4-[6-chloro-4-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxypyridin-3-yl]phenyl]ethanamine
1333		4-[3-(aminomethyl)-6-chloropyridin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
1334		4-[5-(aminomethyl)-6-chloropyridin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
1335		(2S)-2-fluoro-2-[2-[4-fluoro-2-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxyphenyl]pyrimidin-5-yl]ethanamine
1336		(2R)-2-[2-[4-chloro-2-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxyphenyl]pyrimidin-5-yl]-2-fluoroethanamine

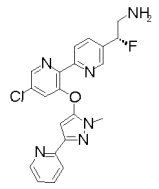
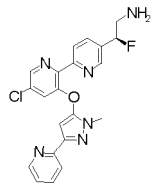
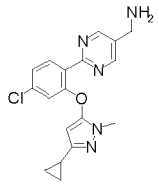
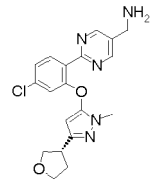
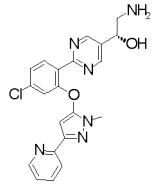
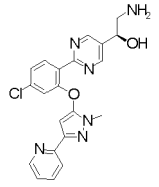
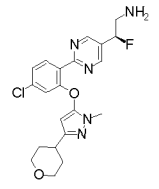
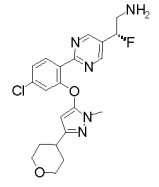
[Table 1-168]

Compound number	Structural formula	Compound name
1337		(2S)-2-[2-[4-chloro-2-(2-methyl-6-morpholin-4-ylpyridin-4-yl) oxyphenyl]pyrimidin-5-yl]-2-fluoroethanamine
1338		(2S)-2-[6-[4-chloro-2-(2-methyl-5-pyridin-2-ylpyrazol-3-yl) oxyphenyl]pyridin-3-yl]-2-fluoroethanamine
1339		(2R)-2-[6-[4-chloro-2-(2-methyl-5-pyridin-2-ylpyrazol-3- yl) oxyphenyl]pyridin-3-yl]-2-fluoroethanamine
1340		[6-[4-chloro-2-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxyphenyl] pyridin-3-yl]methanamine
1341		[2-[4-fluoro-2-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxyphenyl] pyrimidin-5-yl]methanamine
1342		(2R)-2-fluoro-2-[2-[4-fluoro-2-(2-methyl-5-pyridin-2-ylpyrazol-3-yl) oxyphenyl]pyrimidin-5-yl]ethanamine
1343		[6-[5-chloro-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxypyridin-2-yl] pyridin-3-yl]methanamine
1344		(2S)-2-[2-[4-chloro-2-[2-methyl-5-[(3R)-oxolan-3-yl]pyrazol-3-yl] oxyphenyl]pyrimidin-5-yl]-2-fluoroethanamine

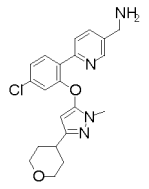
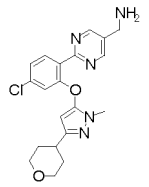
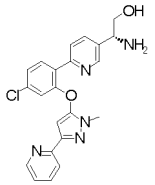
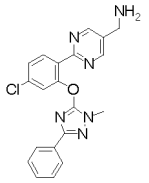
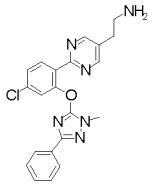
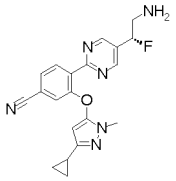
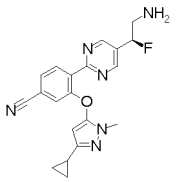
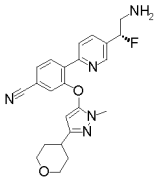
[Table 1-169]

Compound number	Structural formula	Compound name
1345		[6-[4-chloro-2-[2-methyl-5-[(3R)-oxolan-3-yl]pyrazol-3-yl] oxyphenyl]pyridin-3 - yl]methanamine
1346		[6-[4-chloro-2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxyphenyl] pyridin-3- yl]methanamine
1347		(2S)-2-[2-[4-chloro-2-(5-cyclopropyl-2-methylpyrazol-3-yl) oxyphenyl]pyrimidin-5-yl]-2-fluoroethanamine
1348		(2R)-2-[2-[4-chloro-2-(5-cyclopropyl - 2-methylpyrazol-3-yl) oxyphenyl]pyrimidin-5-yl]-2-fluoroethanamine
1349		(1 S)-2-amino-1-[2-[4-chloro-2-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxyphenyl]pyrimidin-5-yl]ethanol
1350		(1R)-2-amino-1-[2-[4-chloro-2-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxyphenyl]pyrimidin-5-yl]ethanol
1351		[2-[5-chloro-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxypyridin-2-yl] pyrimidin-5-yl]methanamine
1352		(2R)-2-[2-[4-chloro-2-[2-methyl-5-[(3R)-oxolan-3-yl]pyrazol-3-yl] oxyphenyl]pyrimidin-5-yl]-2-fluoroethanamine

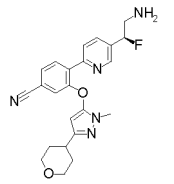
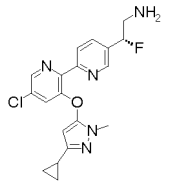
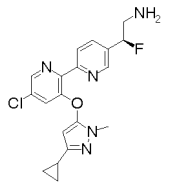
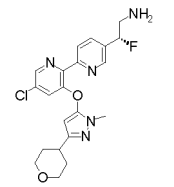
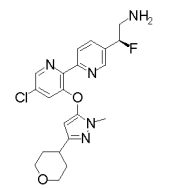
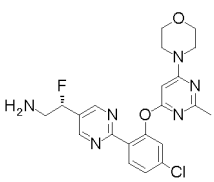
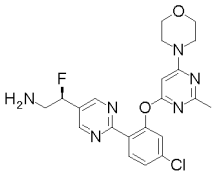
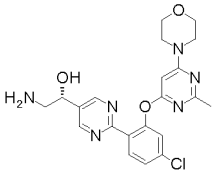
[Table 1-170]

Compound number	Structural formula	Compound name
1353		(2R)-2-[6-[5-chloro-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl) oxypyridin-2-yl]pyridin-3-yl]-2-fluoroethanamine
1354		(2S)-2-[6-[5-chloro-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl) oxypyridin-2-yl]pyridin-3 -yl]-2-fluoroethanamine
1355		[2-[4-chloro-2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxyphenyl] pyrimidin-5-yl]methanamine
1356		[2-[4-chloro-2-[2-methyl-5-[(3 S)-oxolan-3-yl]pyrazol-3-yl]oxyphenyl] pyrimidin-5-yl]methanamine
1357		(1R)-2-amino-1-[2-[4-chloro-2-(2-methyl-5-pyridin-2-ylpyrazol-3-yl) oxyphenyl]pyrimidin-5-yl]ethanol
1358		(1 S)-2-amino-1-[2-[4-chloro-2-(2-methyl-5-pyridin-2-ylpyrazol-3-yl) oxyphenyl]pyrimidin-5-yl]ethanol
1359		(2S)-2-[2-[4-chloro-2-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl]oxyphenyl] pyrimidin-5-yl]-2-fluoroethanamine
1360		(2R)-2-[2-[4-chloro-2-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl]oxyphenyl] pyrimidin-5-yl]-2-fluoroethanamine

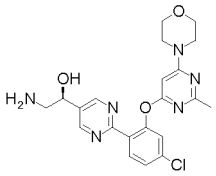
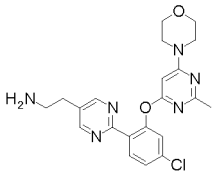
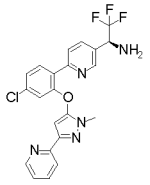
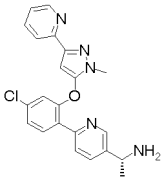
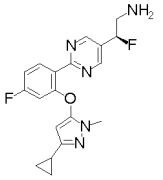
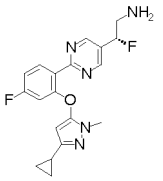
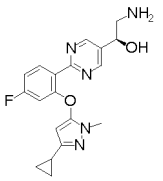
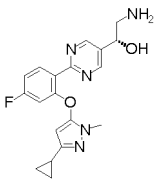
[Table 1-171]

Compound number	Structural formula	Compound name
1361		[6-[4-chloro-2-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl]oxyphenyl]pyridin-3-yl]methanamine
1362		[2-[4-chloro-2-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl]oxyphenyl]pyrimidin-5-yl]methanamine
1363		(2R)-2-amino-2-[6-[4-chloro-2-(2-methyl-5-pyridin-2-ylpyrazol-3-yl) oxyphenyl]pyridin-3-yl]ethanol
1364		[2-[4-chloro-2-[(2-methyl-5-phenyl-1,2,4-triazol-3-yl)oxy]phenyl] pyrimidin-5-yl]methanamine
1365		2-[2-[4-chloro-2-[(2-methyl-5-phenyl-1,2,4-triazol-3-yl)oxy]phenyl] pyrimidin-5-yl]ethanamine
1366		4-[5-[(1R)-2-amino-1-fluoroethyl]pyrimidin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3 - yl)oxybenzonitrile
1367		4-[5-[(1S)-2-amino-1-fluoroethyl]pyrimidin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
1368		4-[5-[(1R)-2-amino-1-fluoroethyl]pyridin-2-yl]-3-[2-methyl-5-(oxan-4-yl) pyrazol-3-yl]oxybenzonitrile

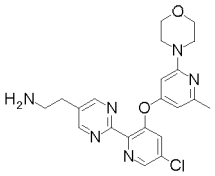
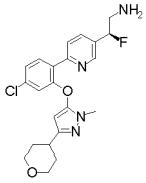
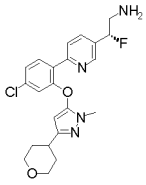
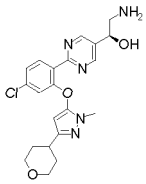
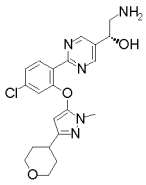
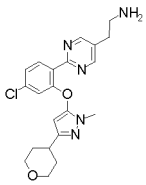
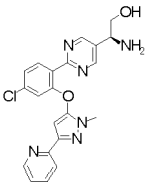
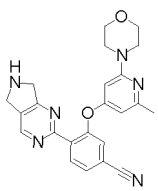
[Table 1-172]

Compound number	Structural formula	Compound name
1369		4-[5-[(1S)-2-amino-1-fluoroethyl]pyridin-2-yl]-3-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl]oxybenzonitrile
1370		(2R)-2-[6-[5-chloro-3-(5-cyclopropyl-2-methylpyrazol-3-yl) oxypyridin-2-yl]pyridin-3-yl]-2-fluoroethanamine
1371		(2S)-2-[6-[5-chloro-3-(5-cyclopropyl-2-methylpyrazol-3-yl) oxypyridin-2-yl]pyridin-3-yl]-2-fluoroethanamine
1372		(2R)-2-[6-[5-chloro-3-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl] oxypyridin-2-yl]pyridin-3-yl]-2-fluoroethanamine
1373		(2S)-2-[6-[5-chloro-3-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl] oxypyridin-2-yl]pyridin-3-yl]-2-fluoroethanamine
1374		(2R)-2-[2-[4-chloro-2-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl) oxyphenyl]pyrimidin-5-yl]-2-fluoroethanamine
1375		(2S)-2-[2-[4-chloro-2-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl) oxyphenyl]pyrimidin-5-yl]-2-fluoroethanamine
1376		(1R)-2-amino-1-[2-[4-chloro-2-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxyphenyl]pyrimidin-5-yl]ethanol

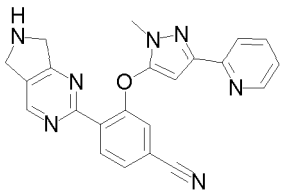
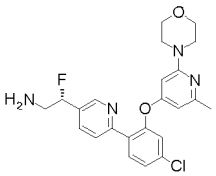
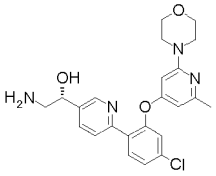
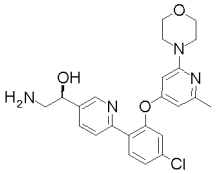
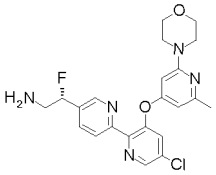
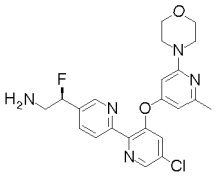
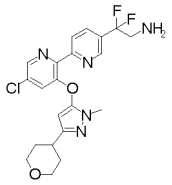
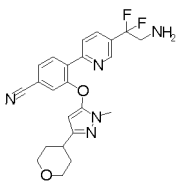
[Table 1-173]

Compound number	Structural formula	Compound name
1377		(1S)-2-amino-1-[2-[4-chloro-2-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxyphenyl]pyrimidin-5-yl]ethanol
1378		2-[2-[4-chloro-2-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl) oxyphenyl]pyrimidin-5-yl]ethanamine
1379		(1S)-1-[6-[4-chloro-2-(2-methyl-5-pyridin-2-ylpyrazol-3-yl) oxyphenyl]pyridin-3-yl]-2,2,2-trifluoroethanamine
1380		(1R)-1-[6-[4-chloro-2-(2-methyl-5-pyridin-2-ylpyrazol-3-yl) oxyphenyl]pyridin-3- yl]ethanamine
1381		(2S)-2-[2-[2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxy-4-fluorophenyl]pyrimidin-5-yl]-2-fluoroethanamine
1382		(2R)-2-[2-[2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxy-4-fluorophenyl]pyrimidin-5-yl]-2-fluoroethanamine
1383		(1S)-2-amino-1-[2-[2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxy-4-fluorophenyl]pyrimidin-5-yl]ethanol
1384		(1R)-2-amino-1-[2-[2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxy-4-fluorophenyl]pyrimidin-5-yl]ethanol

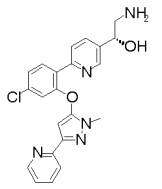
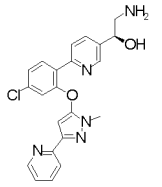
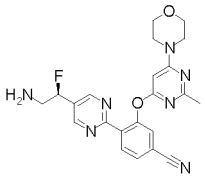
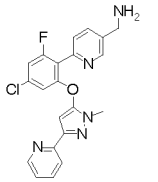
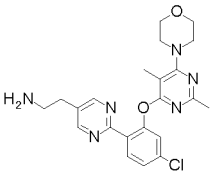
[Table 1-174]

Compound number	Structural formula	Compound name
1385		2-[2-[5-chloro-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxypyridin-2-yl]pyrimidin-5-yl]ethanamine
1386		(2S)-2-[6-[4-chloro-2-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl] oxyphenyl]pyridin-3-yl]-2-fluoroethanamine
1387		(2R)-2-[6-[4-chloro-2-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl] oxyphenyl]pyridin-3-yl]-2-fluoroethanamine
1388		(1 S)-2-amino-1-[2-[4-chloro-2-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl] oxyphenyl]pyrimidin-5-yl]ethanol
1389		(1R)-2-amino-1-[2-[4-chloro-2-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl] oxyphenyl]pyrimidin-5-yl]ethanol
1390		2-[2-[4-chloro-2-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl]oxyphenyl] pyrimidin-5-yl]ethanamine
1391		(2S)-2-amino-2-[2-[4-chloro-2-(2-methyl-5-pyridin-2-ylpyrazol-3-yl) oxyphenyl]pyrimidin-5-yl]ethanol
1392		4-(6,7-dihydro-5H-pyrrolo[3,4-d]pyrimidin-2-yl)-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile

[Table 1-175]

Compound number	Structural formula	Compound name
1393		4-(6,7-dihydro-5H-pyrrolo[3,4-d]pyrimidin-2-yl)-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
1394		(2R)-2-[6-[4-chloro-2-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxyphenyl]pyridin-3-yl]-2-fluoroethanamine
1395		(1R)-2-amino-1-[6-[4-chloro-2-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxyphenyl]pyridin-3-yl]ethanol
1396		(1 S)-2-amino-1-[6-[4-chloro-2-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxyphenyl]pyridin-3-yl]ethanol
1397		(2R)-2-[6-[5-chloro-3 -(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxypyridin-2-yl]pyridin-3-yl]-2-fluoroethanamine
1398		(2S)-2-[6-[5-chloro-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxypyridin-2-yl]pyridin-3-yl]-2-fluoroethanamine
1399		2-[6-[5-chloro-3-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl] oxypyridin-2-yl]pyridin-3-yl]-2,2-difluoroethanamine
1400		4-[5-(2-amino-1,1-difluoroethyl)pyridin-2-yl]-3-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl]oxybenzonitrile

[Table 1-176]

Compound number	Structural formula	Compound name
1401		(1R)-2-amino-1-[6-[4-chloro-2-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxyphenyl]pyridin-3-yl]ethanol
1402		(1S)-2-amino-1-[6-[4-chloro-2-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxyphenyl]pyridin-3-yl]ethanol
1403		4-[5-[(1S)-2-amino-1-fluoroethyl]pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile
1404		[6-[4-chloro-2-fluoro-6-(2-methyl-5-pyridin-2-ylpyrazol-3-yl) oxyphenyl]pyridin-3- yl]methanamine
1405		2-[2-[4-chloro-2-(2,5-dimethyl-6-morpholin-4-ylpyrimidin-4-yl) oxyphenyl]pyrimidin-5-yl]ethanamine

[0056] Among these, preferable compounds are those of compound number 2, 6, 7, 9, 11, 17, 21, 25, 26, 30, 32, 33, 46, 50, 62, 65, 66, 69, 70, 82, 93, 100, 101, 112, 113, 115, 120, 130, 133, 137, 138, 149, 150, 153, 157, 159-162, 164, 170-177, 179, 180, 182, 183, 185-187, 197-199, 202, 204-206, 211-213, 215, 225-233, 237, 238, 241, 246-250, 253, 254, 258, 260-262, 264, 266, 267, 272-278, 285, 287-289, 293-296, 299, 301, 306, 310, 312-315, 317-321, 324-329, 333-338, 341, 344, 346, 348, 360-367, 370-376, 378, 379, 381-384, 388, 390-394, 396, 398, 399, 401-407, 413, 426, 429, 430, 432, 434, 439-441, 444-448, 454, 458, 459, 461, 467, 469-471, 477, 482-485, 493, 496, 498-503, 505-510, 517, 521, 522, 525-527, 529-532, 536, 541-544, 550, 562, 575, 587, 592, 599, 604, 609, 610, 619, 621-629, 634, 637, 642, 644, 651, 652, 655-657, 668, 670-672, 691, 695-697, 701, 702, 704, 706, 708, 711, 714, 715, 718, 724, 734, 735, 737, 742, 743, 748, 754, 758-760, 765, 767-770, 772-775, 786, 787, 795, 799, 801-803, 808-812, 822, 823, 826-828, 832-835, 842, 848-850, 854, 856, 857, 859-861, 866, 872-878, 900, 903-910, 912-916, 932, 935, 937, 945, 948-953, 955, 957, 958, 963, 966, 968, 969, 972, 975, 977-980, 983, 985, 987-992, 996, 1000, 1001, 1010-1014, 1017, 1018, 1025-1033, 1035, 1037, 1042-1049, 1051, 1054, 1057-1063, 1065, 1066, 1071-1080, 1086, 1087, 1097, 1106, 1107, 1110, 1120, 1129-1131, 1135, 1137, 1143-1145, 1147-1156, 1167, 1173, 1184-1187, 1195, 1199, 1202, 1203, 1205-1208, 1210-1212, 1214, 1215, 1217-1219, 1233, 1234, 1237, 1239-1241, 1243, 1244, 1249, 1255, 1258, 1259, 1279, 1280, 1295, 1296, 1299-1302, 1304, 1306, 1312, 1316, 1317, 1322-1325, 1330, 1334, 1335, 1337-1340, 1346, 1348, 1350, 1354, 1357, 1360, 1361, 1366-1369, 1371, 1373, 1380, 1387, 1395, 1398 and 1404, more preferably those of compound number 173, 175, 176, 182, 185, 199, 202, 228-230, 237, 250, 254, 258, 260-262, 264, 272, 274, 275, 277, 285, 288, 289, 293, 295, 299, 310, 317, 319, 324-329, 361-364, 367, 371, 390, 391, 393, 394, 402, 439, 440, 444, 445, 447, 448, 454, 459, 461, 470, 471, 541-543, 592, 599, 609, 621-623, 652, 655-658, 671, 672, 697, 706, 754, 758, 769, 770, 773, 775, 786, 787, 795, 801, 802, 810, 811, 812, 826, 827, 832, 833, 835, 842, 849, 856, 857, 859, 860, 866,

874, 875, 877, 907, 912, 937, 948, 953, 955, 958, 963, 966, 972, 975, 977, 979, 980, 987-991, 1000, 1010, 1012-1014, 1018, 1025-1032, 1037, 1042, 1043, 1051, 1061-1063, 1071-1074.

<General synthesis method>

[0057] The compound represented by the formula (I) of the present invention and a pharmaceutically acceptable salt thereof (hereinafter, these are collectively referred to as the compound of the present invention) can be synthesized by a combination of known methods in the art including the synthesis methods described below. Reagents or solvents described as conditions in the chemical formula are merely examples as described in the description. Each substituent may be protected with a suitable protecting group, if necessary, and may be protected or deprotected at an appropriate step. As a suitable protecting group and a removal method of the protecting group, a protecting group for each substituent and a known method, widely used in this field, can be adopted, and are described, for example, in PROTECTIVE GROUPS in ORGANIC SYNTHESIS, THIRD EDITION, John Wiley&Sons, Inc. Further, the intermediate produced in the following synthesis method may be isolated and purified by a method such as column chromatography, recrystallization, or distillation, or may be used in the next step without isolation.

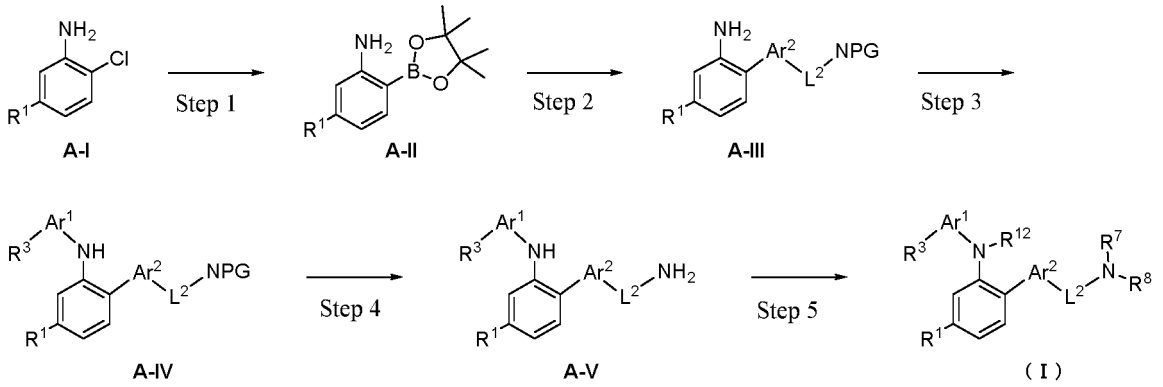
[0058] Typical synthesis methods of the compound of the present invention represented by the general formula (I) will be described below. The synthesis method of the compound of the present invention is not limited to these. The symbols in each formula are defined in the formula (I).

[0059] The compound of the present invention can be produced by several synthesis methods. Hereinafter, a typical synthesis method will be described for each structure of L^1 of the formula (I).

[0060] When L^1 in the formula (I) is $-NR^{12}-$ in the compound of the present invention, the synthesis can be performed by the method, for example as shown in the following reaction scheme, of constructing a biaryl structure with Ar^2 ring and then bonding with Ar^1 ring. That is, (A-I) is converted to a boronic acid ester (A-II), then converted to (A-III) by a Suzuki-Miyaura coupling reaction, and then (A-IV) is obtained by a Buchwald-Hartwig amination reaction. The target compound can be synthesized by deprotecting this compound. The target compound can be also synthesized by modifying the amino group after deprotection.

[0061] In the following reaction scheme, PG is a protecting group for the amino group (the same applies hereinafter).

[Chem. 8]



[0062] Step 1: Bis(pinacolato)diboron is preferable as the borylation reagent, and tris(dibenzylideneacetone)dipalladium, palladium acetate, tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst. If necessary, tricyclohexylphosphine, tricyclohexylphosphonium tetrafluoroborate, 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene or the like is used as the ligand. As the base to be used, potassium acetate or the like is preferable. Here, the solvent is not particularly limited and includes, for example, ethers such as tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 70°C to 120°C.

[0063] Step 2: Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst, and the base includes, for example, inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like. Here, the solvent is not particularly limited,

and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 120°C.

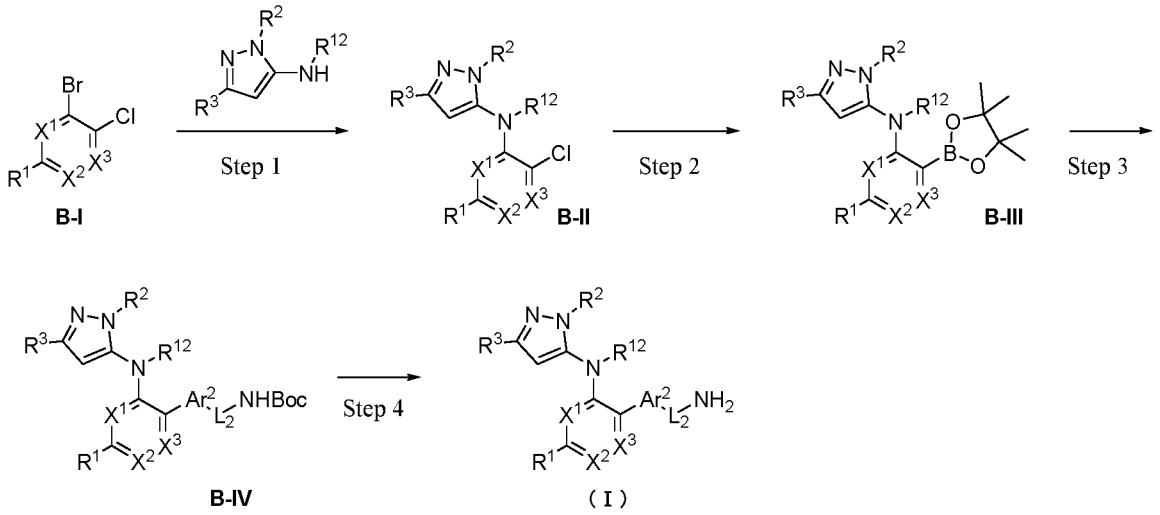
[0064] Step 3: Tris(dibenzylideneacetone)dipalladium, palladium acetate or the like is preferable as the palladium catalyst. 4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene, 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl, 2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl or the like is preferable as the ligand. The base includes inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like, potassium tert-butoxide, sodium tert-butoxide and the like. Here, the solvent is not particularly limited, and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 150°C.

[0065] Step 4: As a removal method of the protecting group, a known method widely used in this field can be adopted. For example, when the protecting group is a Boc group, a strong acid such as trifluoroacetic acid, hydrochloric acid or sulfuric acid is preferable, and when the protecting group is phthalimide, hydrazine, ethylenediamine or the like is preferable. Here, the solvent is not particularly limited, and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide and the like. The reaction temperature is preferably from 0°C to 100°C.

[0066] Step 5: The reaction can be performed using an alkyl halide or the like as a reagent having a leaving group. The base includes organic bases such as triethylamine, N,N-diisopropylethylamine, and the like, and inorganic bases such as potassium carbonate, cesium carbonate, and the like. Tetrahydrofuran, N,N-dimethylformamide, dimethyl sulfoxide or the like is preferable as the solvent. The reaction temperature is preferably from 0°C to 120°C, and particularly preferable from 0°C to room temperature. When X^1, X^2 and X^3 in the formula (I) are CH, the synthesis is performed in the above reaction scheme, while even the compound wherein at least one of X^1, X^2 and X^3 is N or CY (wherein Y is a halogen atom or a methyl group) can be synthesized in the same method.

[0067] When L^1 in the formula (I) is $-NR^{12}-$ in the compound of the present invention, synthesis can be performed by the method, for example as shown in the following reaction scheme, of reacting with Ar^1 ring having an amino group and constructing the L^1 linker moiety, and then forming a biaryl bond with Ar^2 ring.

[Chem. 9]



[0068] Step 1: Tris(dibenzylideneacetone)dipalladium, palladium acetate or the like is preferable as the palladium catalyst. 4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene, 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl, 2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl or the like is preferable as the ligand. The base includes inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium

carbonate, tripotassium phosphate, and the like, potassium tert-butoxide, sodium tert-butoxide and the like. Here, the solvent is not particularly limited, and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 150°C.

[0069] Step 2: Bis(pinacolato)diboron is preferable as the borylation reagent and tris(dibenzylideneacetone)dipalladium, palladium acetate, tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst. If necessary, tricyclohexylphosphine, tricyclohexylphosphonium tetrafluoroborate, 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene or the like is used as the ligand. The base to be used include potassium acetate and the like. Here, the solvent is not particularly limited, and include, for example, ethers such as tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 70°C to 120°C.

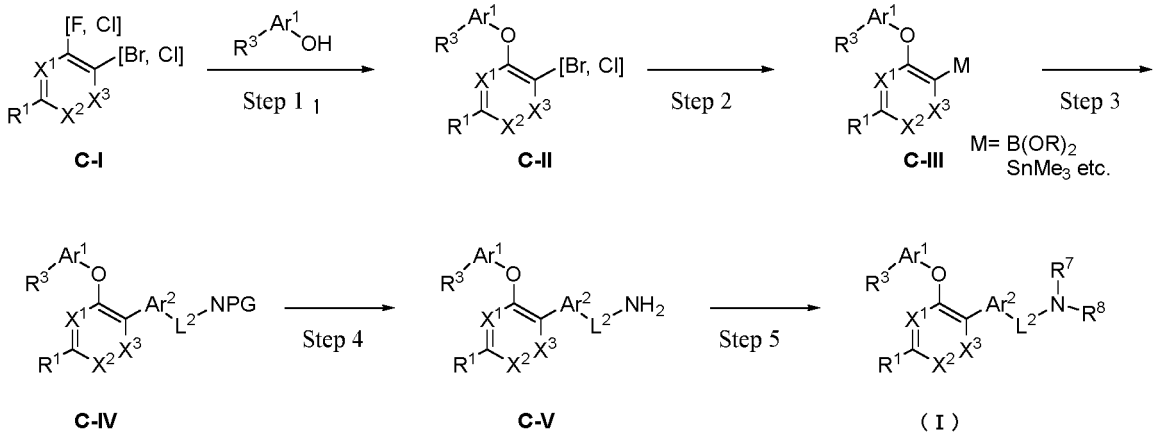
[0070] Step 3: Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst, and the base includes, for example, inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N, N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 120°C.

[0071] Step 4: A strong acid such as trifluoroacetic acid, hydrochloric acid, sulfuric acid, or the like is preferable as the reagent, and a solvent such as dichloromethane, tetrahydrofuran, ethyl acetate or the like is preferable as the solvent. The reaction temperature is preferably from 0°C to 50°C, and particularly preferably from 0°C to room temperature.

[0072] When L^1 in the formula (I) is -O- in the compound of the present invention, synthesis can be performed by using the following synthesis methods.

[0073] For example, the synthesis can be performed by the method shown in the following reaction scheme. That is, by obtaining (C-II) bonding with Ar^1 ring via an oxygen atom by nucleophilic aromatic substitution reaction, converting (C-II) into a boron compound, a tin compound, or the like, and by performing the cross-coupling reaction with the corresponding Ar^2 ring compound, the biaryl form (C-IV) can be synthesized. After that, if the amino group is protected, the deprotection thereof can be performed, and if necessary, the target compound can be synthesized by modification of a free amino group. On the other hand, (C-II) can be directly used to perform cross-coupling reaction or the like with Ar^2 ring compounds having suitable reactive substituents without an operation of step 2. Further, substituent R^3 can be converted at an appropriate timing in the following reaction scheme by methods known to those skilled in the art, depending on a target structure.

[Chem. 10]



[0074] Step 1: Potassium carbonate, sodium carbonate, cesium carbonate, potassium tert-butoxide, sodium tert-butoxide or the like is preferable as the base to be used. Preferred solvents include, for example, N,N-dimethylformamide, N,N-dimethylacetamide, N-methylpyrrolidone, dimethyl sulfoxide and the like. The reaction temperature is preferably

from room temperature to 150°C.

[0075] Step 2: The borylation reagent to be used includes, for example, bis(pinacolato)diboron and the like, and the tin reagent includes, for example, hexamethylditin and the like. Tris(dibenzylideneacetone)dipalladium, palladium acetate, tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst. If necessary, tricyclohexylphosphine, tricyclohexylphosphonium tetrafluoroborate, 4,5-bis (diphenylphosphino)-9,9-dimethylxanthene or the like is used as the ligand. Potassium acetate or the like is preferable as the base for borylation. Here, the solvent is not particularly limited, and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 70°C to 120°C.

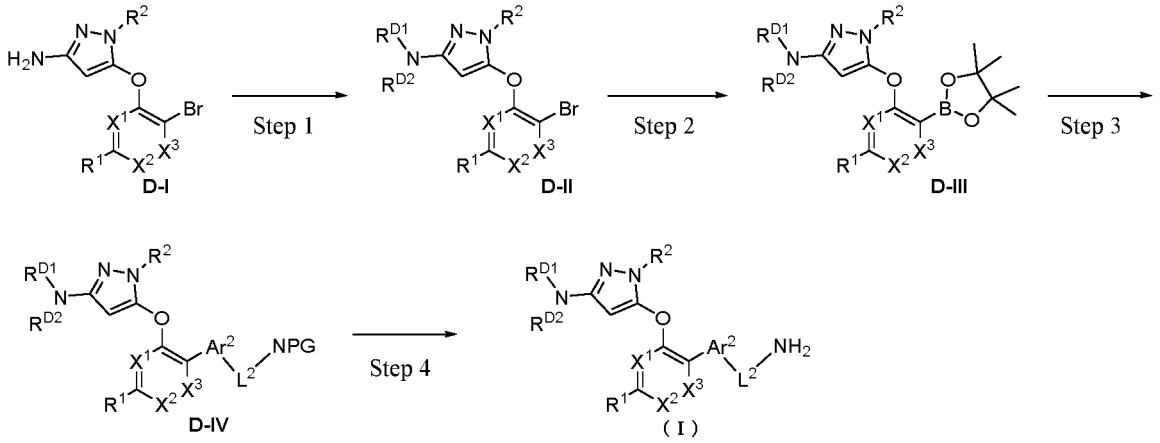
[0076] Step 3: Tetrakis(triphenylphosphine)palladium(0), bis(triphenylphosphine)palladium(II) dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium(II) dichloride or the like is preferable as the palladium catalyst, and the base includes, for example, inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 120°C.

[0077] Step 4: As a removal method of the protecting group, a known method widely used in this field can be adopted. For example, when the protecting group is a Boc group, a strong acid such as trifluoroacetic acid, hydrochloric acid or sulfuric acid is preferable, and when the protecting group is phthalimide, hydrazine or ethylenediamine or the like is preferable. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide and the like. The reaction temperature is preferably from 0°C to 100°C.

[0078] Step 5: Alkyl halide or the like can be used for the reaction as a reaction reagent having a leaving group. The base includes, for example, organic bases such as triethylamine, N,N-diisopropylethylamine and the like, and inorganic bases such as potassium carbonate, cesium carbonate and the like. Tetrahydrofuran, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide or the like is preferable as the solvent. The reaction temperature is preferably from 0°C to 120°C.

[0079] When L^1 in the formula (I) is -O- in the compound of the present invention, the target compound can be also synthesized using the intermediate pyrazole (D-I) as shown in the following reaction scheme. That is, after reacting (D-I) with a reagent having a leaving group and modifying the amino group to obtain (D-II), the target compound can be synthesized by the same method as described above.

[Chem. 11]



(Wherein, R^{D1} and R^{D2} are substituents that form $-NR^{D1}R^{D2}$ to satisfy R^3 in the formula (I))

[0080] Step 1: Reaction reagent having a leaving group includes, for example, alkyl halides and alkyl triflate and the like. Organic bases such as triethylamine and N,N-diisopropylethylamine, inorganic bases such as potassium carbonate and cesium carbonate or the like is preferable as the base. If necessary, an additive such as potassium iodide may be added. 1,4-Dioxane, N,N-dimethylformamide, N,N-dimethylacetamide, N-methylpyrrolidone or the like is preferable as the solvent. The reaction temperature is preferably from room temperature to 150°C, and particularly preferably from 50°C to 120°C.

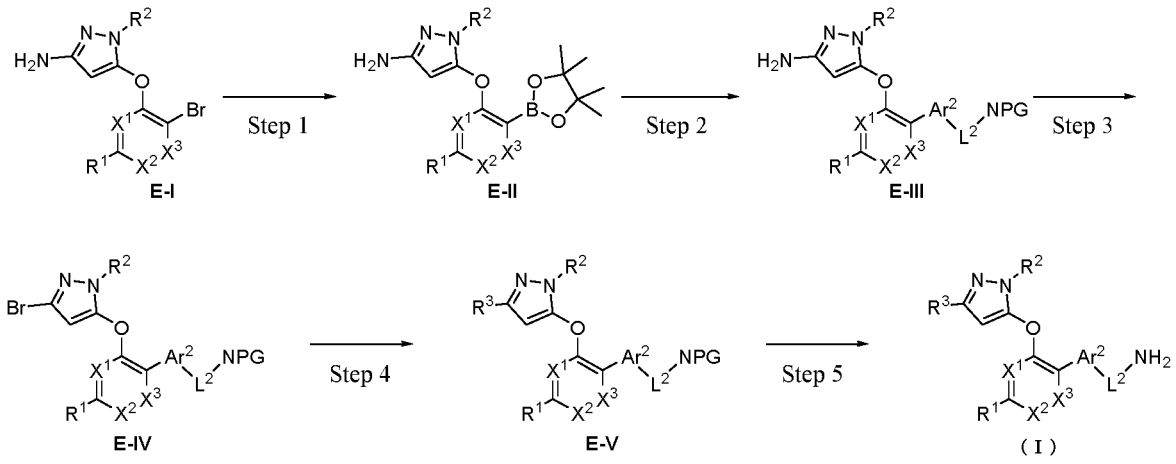
[0081] Step 2: The borylation reagent includes, for example, bis(pinacolato)diboron and the like. Tris(dibenzylideneacetone)dipalladium, palladium acetate, tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst. If necessary, tricyclohexylphosphine, tricyclohexylphosphonium tetrafluoroborate, 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene or the like is used as the ligand. Potassium acetate or the like is preferable as the base to be used. Here, the solvent is not particularly limited and includes, for example, ethers such as tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 70°C to 120°C.

[0082] Step 3: Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst, and the base includes, for example, inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 120°C.

[0083] Step 4: As a removal method of the protecting group, a known method widely used in this field can be adopted. For example, when the protecting group is a Boc group, a strong acid such as trifluoroacetic acid, hydrochloric acid, sulfuric acid, or the like is preferable, and when the protecting group is phthalimide, hydrazine, ethylenediamine or the like is preferable. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide and the like. The reaction temperature is preferably from 0°C to 100°C.

[0084] When L^1 in the formula (I) is -O- in the compound of the present invention, the target compound can be also synthesized, as shown in the following reaction scheme, by constructing a biaryl bond with Ar^2 ring, then converting the amino group in (E-III) to a bromine atom, and introducing R^3 substituent by, for example, cross-coupling reaction.

[Chem. 12]



[0085] Step 1: Bis(pinacolato)diboron is preferable as the borylation reagent, and tris(dibenzylideneacetone)dipalladium, palladium acetate, tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst. If necessary,

tricyclohexylphosphine, tricyclohexylphosphonium tetrafluoroborate, 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene or the like is used as the ligand. Potassium acetate or the like is preferable as the base to be used. Here, the solvent is not particularly limited and includes, for example, ethers such as tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 70°C to 120°C.

[0086] Step 2: Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst, and the base includes, for example, inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 120°C.

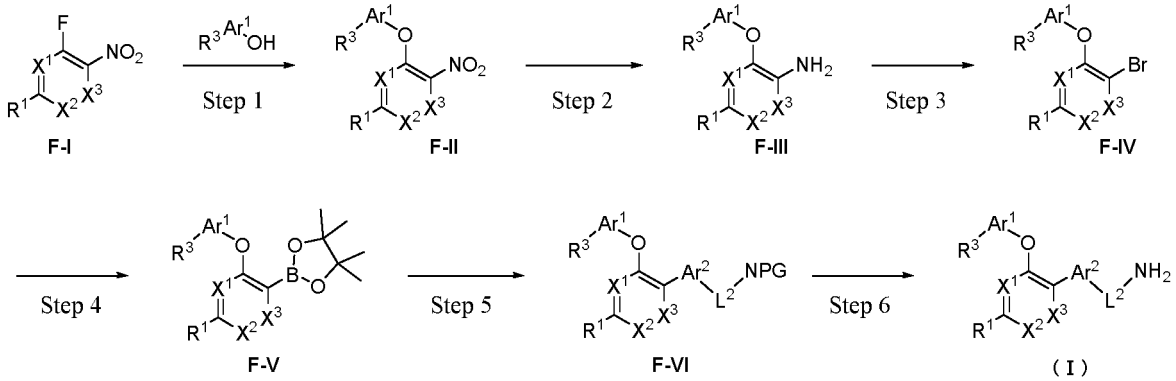
[0087] Step 3: Isoamyl nitrite is preferable as the reagent to be used, and copper bromide or the like is preferable as the bromination reagent. Preferred solvents include acetonitrile, toluene, and the like. The reaction temperature is preferably from 0°C to 50°C.

[0088] Step 4: Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst, and the base includes, for example, inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 120°C.

[0089] Step 5: As a removal method of the protecting group, a known method widely used in this field can be adopted. For example, when the protecting group is a Boc group, a strong acid such as trifluoroacetic acid, hydrochloric acid, sulfuric acid, or the like is preferable, and when the protecting group is phthalimide, hydrazine, ethylenediamine or the like is preferable. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide and the like. The reaction temperature is preferably from 0°C to 100°C.

[0090] When L^1 in the formula (I) is -O- in the compound of the present invention, the target compound can be also synthesized, as shown in the following reaction scheme, by performing an aromatic nucleophilic substitution reaction using a raw material (F-I) having a nitro group, then converting the functional group of the nitro group, followed by a biaryl bond formation with Ar^2 ring.

[Chem. 13]



[0091] Step 1: Potassium carbonate, sodium carbonate, cesium carbonate, potassium tert-butoxide, sodium tert-butoxide or the like is preferable as the base to be used. Preferred solvents include N,N-dimethylformamide, N,N-

dimethylacetamide, N-methylpyrrolidone, dimethyl sulfoxide and the like. The reaction temperature is preferably from room temperature to 100°C.

[0092] Step 2: Iron, zinc, or the like is preferable as the metal reagent to be used, and is preferably used in combination with a reagent such as ammonium chloride, acetic acid, or the like. Preferred solvents include organic solvents such as ethanol, methanol, tetrahydrofuran, and the like, mixed solvents obtained by adding water thereto, and the like. The reaction temperature is preferably from room temperature to 100°C.

[0093] Step 3: Isoamyl nitrite is preferable as the reagent to be used, and copper bromide or the like is preferable as the bromination reagent. Preferred solvents include acetonitrile, toluene, and the like. The reaction temperature is preferably from 0°C to 50°C.

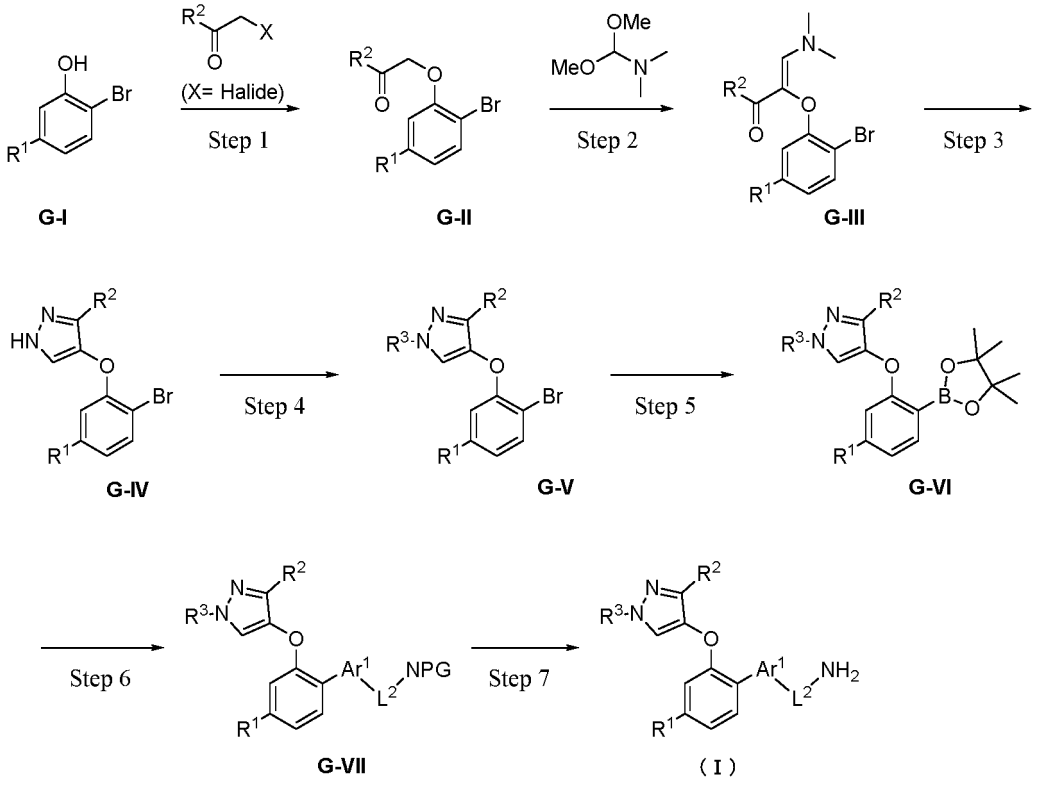
[0094] Step 4: Bis(pinacolato)diboron is preferable as the borylation reagent, and tris(dibenzylideneacetone)dipalladium, palladium acetate, tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst. If necessary, tricyclohexylphosphine, tricyclohexylphosphonium tetrafluoroborate, 4,5-bis(diphenylphosphino) -9,9-dimethylxanthene or the like is used as the ligand. Potassium acetate or the like is preferable as the base to be used. Here, the solvent is not particularly limited and includes, for example, ethers such as tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 70°C to 120°C.

[0095] Step 5: Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst and the base includes, for example, inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 120°C.

[0096] Step 6: As a removal method of the protecting group, a known method widely used in this field can be adopted. For example, when the protecting group is a Boc group, a strong acid such as trifluoroacetic acid, hydrochloric acid or sulfuric acid is preferable, and when the protecting group is phthalimide, hydrazine, ethylenediamine or the like is preferable. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from 0°C to 100°C.

[0097] When L^1 in the formula (I) is -O- in the compound of the present invention, the target compound can be also synthesized, using the intermediate pyrazole (G-IV) obtained through the cyclization reaction, as shown in the following reaction scheme. That is, after reacting a reagent having a leaving group with pyrazole (G-IV) obtained in three steps from the starting material (G-I) to introduce R^3 substituent, the target compound can be synthesized by the same method as described above.

[Chem. 14]



[0098] Step 1: Potassium carbonate, sodium carbonate, cesium carbonate, potassium tert-butoxide, sodium tert-butoxide or the like is preferable as the base to be used. Preferred solvents include N,N-dimethylformamide, N,N-dimethylacetamide, N-methylpyrrolidone, dimethyl sulfoxide and the like. The reaction temperature is preferably from room temperature to 100°C.

[0099] Step 2: This reaction is preferably performed without solvent. The reaction temperature is preferably from 50°C to 100°C.

[0100] Step 3: The reaction is performed using hydrazine monohydrate as a reagent. Acetic acid or the like is preferable as the solvent. The reaction temperature is preferably from 70°C to 120°C.

[0101] Step 4: The reaction reagent having a leaving group includes, for example, alkyl halides, aryl halides, and the like. Organic bases such as triethylamine and N,N-diisopropylethylamine, and the like, inorganic bases such as potassium carbonate and cesium carbonate, and the like are preferable as the base. Here, the solvent is not particularly limited and includes, for example, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from room temperature to 150°C.

[0102] Step 5: Bis(pinacolato)diboron is preferable as the borylation reagent, and tris(dibenzylideneacetone)dipalladium, palladium acetate, tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst. If necessary, tricyclohexylphosphine, tricyclohexylphosphonium tetrafluoroborate, 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene or the like is used as the ligand. Potassium acetate or the like is preferable as the base to be used. Here, the solvent is not particularly limited and includes, for example, ethers such as tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 70°C to 120°C.

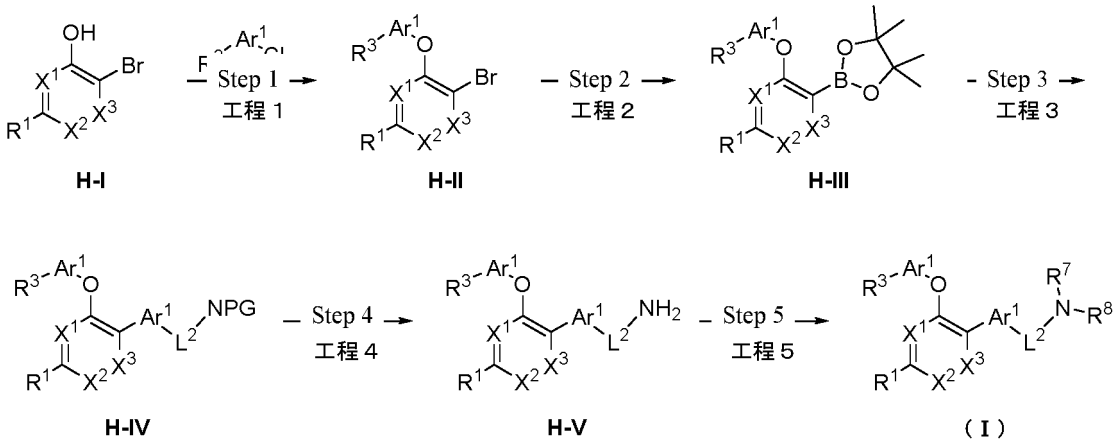
[0103] Step 6: Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst, and the base includes, for example, inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water, mixed

solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 120°C.

[0104] Step 7: As a removal method of the protecting group, a known method widely used in this field can be adopted. For example, when the protecting group is a Boc group, a strong acid such as trifluoroacetic acid, hydrochloric acid or sulfuric acid is preferable, and when the protecting group is phthalimide, hydrazine, ethylenediamine or the like is preferable. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from 0°C to 100°C.

[0105] When L^1 in the formula (I) is -O- in the compound of the present invention, an aromatic nucleophilic substitution reaction or the like can be also performed using a substrate having a leaving group in Ar^1 ring as shown in the following reaction scheme. (H-IV) can be synthesized by reacting (H-II) directly with Ar^2 ring compounds having suitable reactive substituents without an operation of step 2. Substituent R^3 (e.g., a halogen atom) can be converted to a target structure at an appropriate timing in the following reaction scheme by a method known to those skilled in the art, depending on a target structure.

[Chem. 15]



[0106] Step 1: Potassium carbonate, sodium carbonate, cesium carbonate, potassium tert-butoxide, sodium tert-butoxide or the like is preferable as the base to be used. Preferred solvents include N,N-dimethylformamide, N,N-dimethylacetamide, N-methylpyrrolidone, dimethyl sulfoxide and the like. The reaction temperature is preferably from room temperature to 150°C.

[0107] Step 2: Bis(pinacolato)diboron is preferable as the borylation reagent, and tris(dibenzylideneacetone)dipalladium, palladium acetate, tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst. If necessary, tricyclohexylphosphine, tricyclohexylphosphonium tetrafluoroborate, 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene or the like is used as the ligand. Potassium acetate or the like is preferable as the base to be used. Here, the solvent is not particularly limited and includes, for example, ethers such as tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, N, N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, a mixed solvent thereof, and the like. The reaction temperature is preferably 50°C to 150°C, and particularly preferably from 70°C to 120°C.

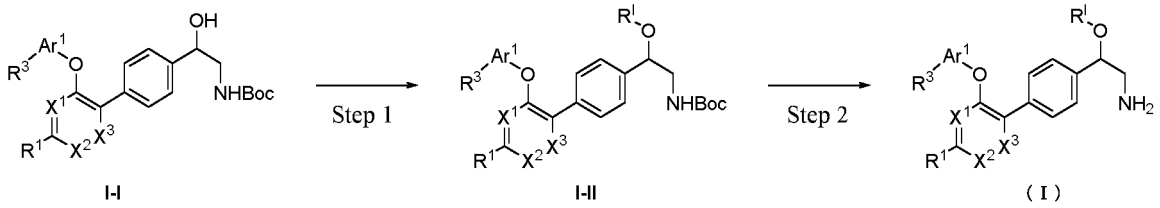
[0108] Step 3: Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst, and the base includes, for example, inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water, mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 120°C.

[0109] Step 4: As a removal method of the protecting group, a known method widely used in this field can be adopted. For example, when the protecting group is a Boc group, a strong acid such as trifluoroacetic acid, hydrochloric acid or sulfuric acid is preferable, and when the protecting group is phthalimide, hydrazine, ethylenediamine or the like is preferable. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from 0°C to 100°C.

[0110] Step 5: The reaction reagent having a leaving group includes, for example, alkyl halides and aryl triflate, and the like. The base includes, for example, organic bases such as triethylamine, N,N-diisopropylethylamine and the like, and inorganic bases such as potassium carbonate, cesium carbonate and the like. Tetrahydrofuran, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide or the like is preferable as the solvent. The reaction temperature is preferably from 0°C to 120°C.

[0111] When L^1 in the formula (I) is -O- in the compound of the present invention, the target compound can be synthesized by modifying the compound (I-I) having an alcohol as shown in the following reaction scheme.

[Chem. 16]



I-I I-II (I)

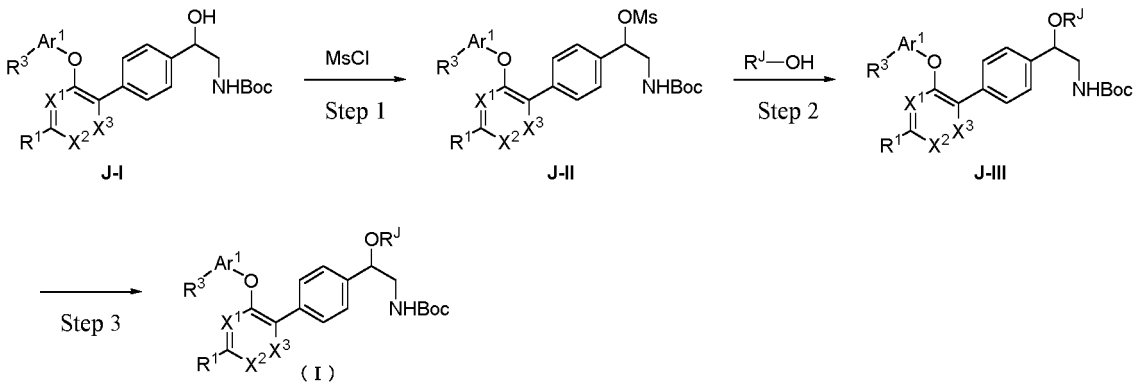
(Wherein, R^1 is a substituent which forms $-OR^I$ to satisfy R^{21} in the formula (I).)

[0112] Step 1: The reaction reagent having a leaving group includes, for example, alkyl halides and alkyl triflate and the like. Sodium hydride, potassium carbonate, cesium carbonate or the like is preferable as the base. Here, the solvent is not particularly limited and includes, for example, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from 0°C to 120°C.

[0113] Step 2: Trifluoroacetic acid, hydrochloric acid, sulfuric acid, or the like is preferable as the strong acid to be used, and a solvent such as dichloromethane, tetrahydrofuran, ethyl acetate and the like is preferable as the solvent. The reaction temperature is preferably from 0°C to 50°C, and particularly preferably from 0°C to room temperature.

[0114] When L^1 in the formula (I) is -O- in the compound of the present invention, after converting the alcohol in (J-I) to a leaving group to introduce an alkoxy group as shown in the following reaction scheme, the target compound can also be synthesized by the same method as described above.

[Chem. 17]



J-I J-II J-III (I)

(Wherein,

Ms is a methanesulfonyl group;

R^J is a substituent which forms $-OR^J$ to satisfy R^{21} in the formula (I).)

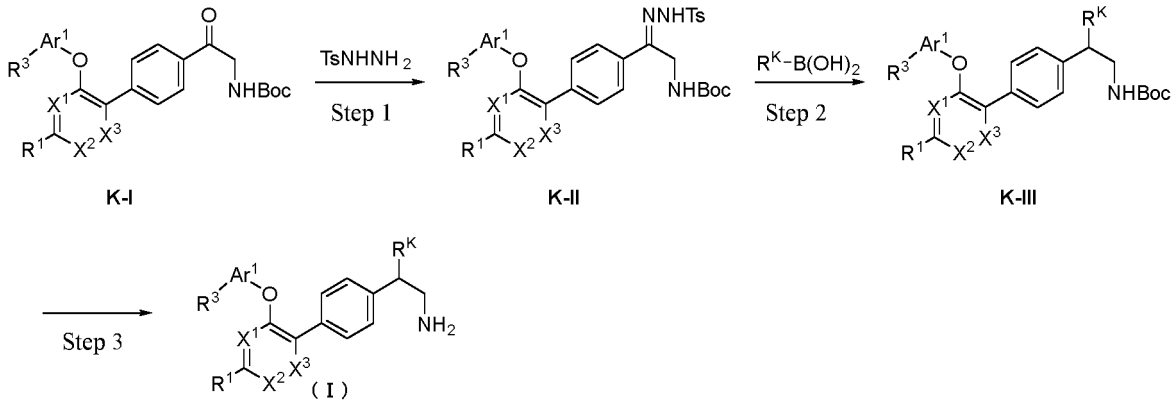
[0115] Step 1: As the mesylation reagent, methanesulfonyl chloride can be used to perform the reaction. Triethylamine, potassium carbonate, cesium carbonate or the like is preferable as the base. The solvent is not particularly limited in this reaction and includes, for example, organic solvents such as tetrahydrofuran, dichloromethane, and the like. This reaction is performed preferably at 0°C to 60°C, and particularly preferably at 0°C to room temperature.

[0116] Step 2: An alcohol (R^J-OH) corresponding to the target compound can be used to perform the reaction. As preferred bases, inorganic bases such as sodium hydride, potassium carbonate, cesium carbonate, and the like can be used. The solvent in this reaction includes, for example, organic solvents such as tetrahydrofuran, N,N-dimethylformamide, N,N-dimethylacetamide, N-methylpyrrolidone, and the like, or a mixed solvent thereof. This reaction is performed preferably at room temperature to 150°C, and particularly preferably at room temperature to 100°C.

[0117] Step 3: Trifluoroacetic acid, hydrochloric acid, sulfuric acid, or the like is preferable as the strong acid to be used, and a solvent such as dichloromethane, tetrahydrofuran, ethyl acetate or the like is preferable as the solvent. The reaction temperature is preferably from 0°C to 50°C, and particularly preferably from 0°C to room temperature.

[0118] When L^1 in the formula (I) is -O- in the compound of the present invention, after introducing the target substituent via tosylhydrazone (K-II) as described in the following reaction scheme, synthesis can be performed by the same method as described above.

[Chem. 18]



(Wherein,

Ts is a p-toluenesulfonyl group;

R^K is a C_{1-3} alkoxy-C_{1-3} alkyl group, a hydroxy(C_{1-6} alkyl) group, a hydroxycarbonyl-(C_{1-3} alkyl) group, a (C_{1-3} alkoxy)carbonyl-(C_{1-3} alkyl) group, or a phenyl group optionally substituted with 1 to 3 halogen atoms.)

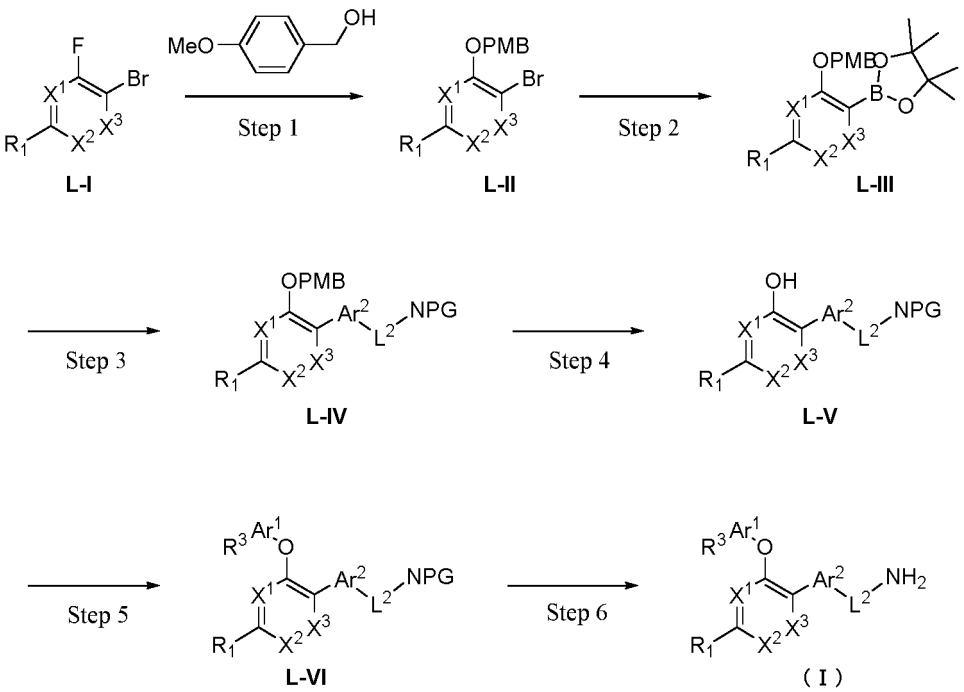
[0119] Step 1: Tosylhydrazine is used as a reagent in this reaction. Preferred solvents include toluene, methanol, ethanol, and the like. The reaction temperature is preferably from room temperature to 120°C, and particularly preferably from 50°C to 120°C.

[0120] Step 2: Potassium carbonate, cesium carbonate, cesium fluoride or the like is preferable as the base to be used. Here, the solvent is not particularly limited and includes, for example, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane and the like. The reaction temperature is preferably from room temperature to 150°C, and particularly preferably from 80°C to 120°C.

[0121] Step 3: Trifluoroacetic acid, hydrochloric acid, sulfuric acid, or the like is preferable as the strong acid to be used, and a solvent such as dichloromethane, tetrahydrofuran, ethyl acetate or the like is preferable as the solvent. The reaction temperature is preferably from 0°C to 50°C, and particularly preferably from 0°C to room temperature.

[0122] When L^1 in the formula (I) is -O- in the compound of the present invention, synthesis can be performed also by a method described in the following reaction scheme. That is, the target compound can be synthesized by the following steps: the raw material (L-I) is reacted with paramethoxybenzyl alcohol to obtain compound (L-II); subsequently, the biaryl compound (L-IV) is obtained through functional group conversion of the bromine atom in (L-II), and then the PMB group is deprotected to lead to phenol (L-V); after linking this phenol (L-V) with Ar^1 compound having a reactive substituent by an appropriate reaction, an amino group is deprotected.

[Chem. 19]



[0123] Step 1: Potassium carbonate, sodium carbonate, cesium carbonate, potassium tert-butoxide, sodium tert-butoxide or the like is preferable as the base to be used. Preferred solvents include N,N-dimethylformamide, N,N-dimethylacetamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from room temperature to 100°C.

[0124] Step 2: Bis(pinacolato)diboron is preferable as the borylation reagent to be used, and tris(dibenzylideneacetone)dipalladium, palladium acetate, tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst. If necessary, tricyclohexylphosphine, tricyclohexylphosphonium tetrafluoroborate, 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene or the like is used as the ligand. Potassium acetate or the like is preferable as the base to be used. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 70°C to 120°C.

[0125] Step 3: Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst, and the base includes, for example, inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 120°C.

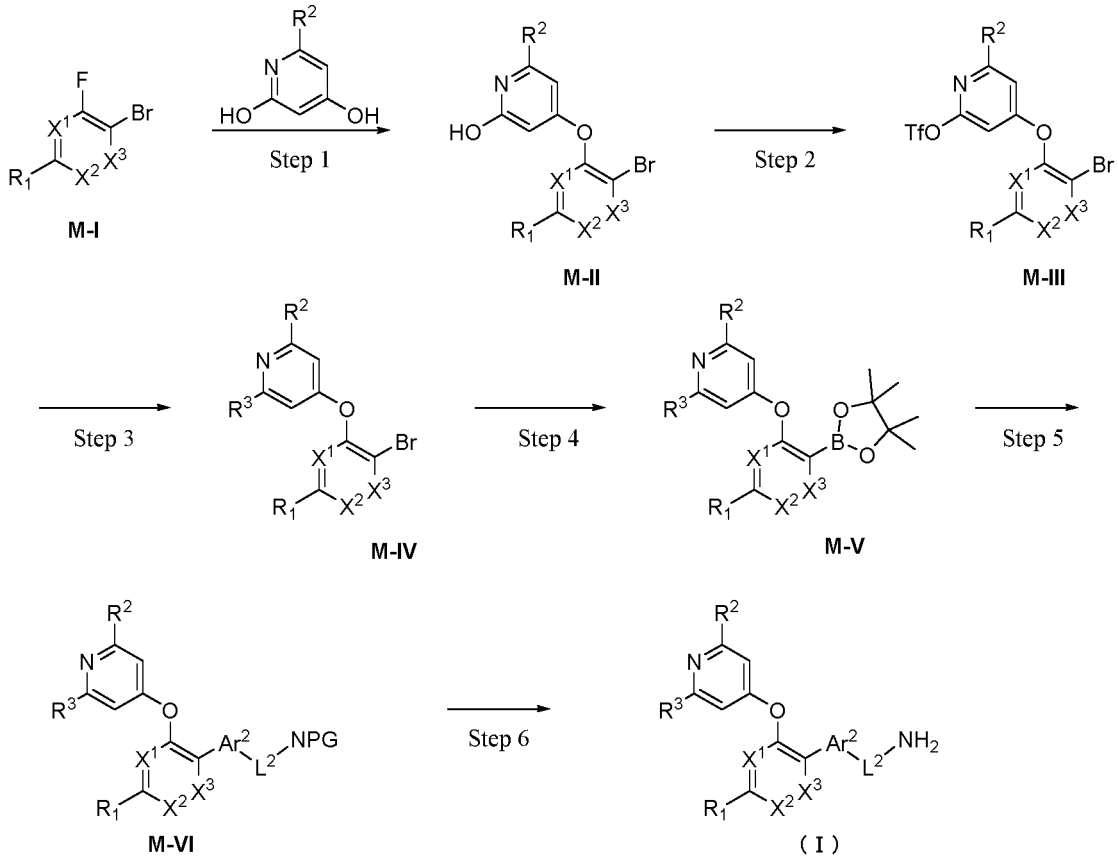
[0126] Step 4: As a removal method of the paramethoxybenzyl group, a known method can be adopted. For example, strong acids include such as trifluoroacetic acid, hydrochloric acid, sulfuric acid, and the like, and the solvent is not particularly limited and includes, for example, tetrahydrofuran, 1,4-dioxane, dichloromethane and the like. The reaction temperature is preferably from 0°C to 100°C.

[0127] Step 5: Potassium carbonate, sodium carbonate, cesium carbonate, potassium tert-butoxide, sodium tert-butoxide or the like is preferable as the base to be used. Preferred solvents include N,N-dimethylformamide, N,N-dimethylacetamide, N-methylpyrrolidone, dimethyl sulfoxide and the like. The reaction temperature is preferably from room temperature to 150°C.

[0128] Step 6: As a removal method of the protecting group, a known method widely used in this field can be adopted. For example, when the protecting group is a Boc group, a strong acid such as trifluoroacetic acid, hydrochloric acid or sulfuric acid is preferable, and when the protecting group is phthalimide, hydrazine, ethylenediamine or the like is preferable. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide and the like. The reaction temperature is preferably from 0°C to 100°C.

[0129] When L^1 in the formula (I) is -O- in the compound of the present invention, synthesis can be performed also by a method described in the following reaction scheme. That is, the target compound can be synthesized by the following steps: 2,4-dihydroxy-6-methylpyridine is reacted with the raw material (M-I) to obtain compound (M-II); subsequently, (M-II) is triflated, and then the target R^3 substituents is introduced thereto to give (M-IV); subsequently, the biaryl compound (M-VI) is obtained through functional group conversion of the bromine atom in (M-IV), and then the amino group is deprotected.

[Chem. 20]



[0130] Step 1: Potassium carbonate, sodium carbonate, cesium carbonate, potassium tert-butoxide, sodium tert-butoxide or the like is preferable as the base to be used. Preferred solvents include N,N-dimethylformamide, N,N-dimethylacetamide, N-methylpyrrolidone, dimethyl sulfoxide and the like. The reaction temperature is preferably from room temperature to 160°C.

[0131] Step 2: The triflation agent to be used includes trifluoromethanesulfonic anhydride (TfzO) and the like, and pyridine, triethylamine, N,N-diisopropylethylamine or the like is preferable as the base. Preferred solvents include tetrahydrofuran, dichloromethane, 1,2-dichloroethane and the like. The reaction temperature is preferably from 0°C to 100°C.

[0132] Step 3: As a method for introducing R^3 substituent, a known method commonly used in the art can be adopted. For example, in the case of introducing R^3 substituent using boronic acid derivatives, tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst, and the base includes, for example, inorganic salts such as sodium hydroxide,

potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 120°C.

[0133] Further, for example, in the case of reacting with an alcohol or an amine corresponding to R^3 substituent, preferred base includes, for example, organic bases such as triethylamine and N,N-diisopropylethylamine, an inorganic base such as potassium carbonate and cesium carbonate and the like. Here, the solvent is not particularly limited and includes, for example, ethers such as tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide and the like. The reaction temperature is preferably from room temperature to 150°C.

[0134] Step 4: Bis(pinacolato)diboron is preferable as the borylation reagent to be used, and tris(dibenzylideneacetone)dipalladium, palladium acetate, tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst. If necessary, tricyclohexylphosphine, tricyclohexylphosphonium tetrafluoroborate, 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene or the like is used as the ligand. The base to be used includes potassium acetate and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 70°C to 120°C.

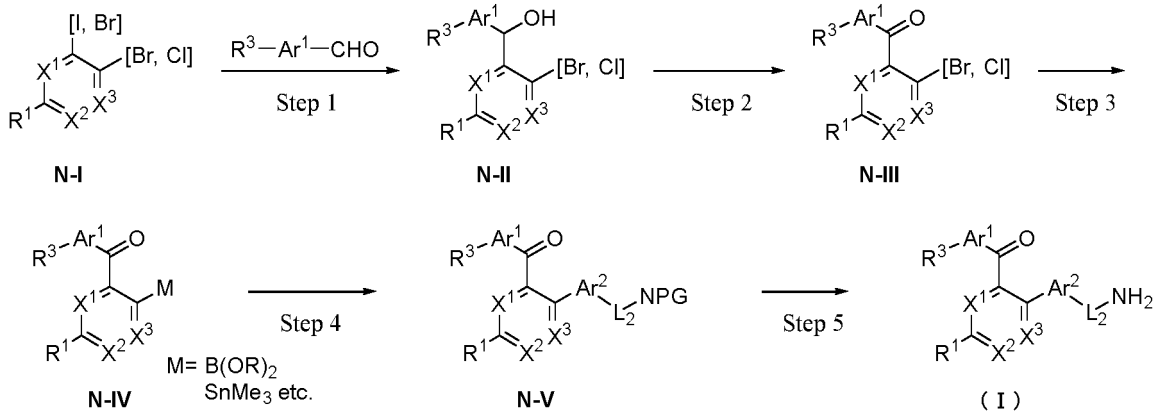
[0135] Step 5: Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst, and the base includes, for example, inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 120°C.

[0136] Step 6: As a removal method of the protecting group, a known method widely used in this field can be adopted. For example, when the protecting group is a Boc group, a strong acid such as trifluoroacetic acid, hydrochloric acid, sulfuric acid, or the like is preferable, and when the protecting group is phthalimide, hydrazine, ethylenediamine or the like is preferable. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from 0°C to 100°C.

[0137] When L^1 in the formula (I) is -CO- in the compound of the present invention, the synthesis can be performed by using the following synthesis methods.

[0138] For example, the synthesis can be performed by the method shown in the following reaction scheme. That is, an Ar^1 ring compound having an aldehyde is reacted with an anionic reagent prepared from the compound (N-I) to synthesize a corresponding alcohol (N-II), which is further oxidized to give a ketone (N-III). Subsequently, a biaryl bond can be formed to synthesize (N-V). Further, R^3 substituent can be converted at an appropriate timing in the following reaction scheme by a method known to those skilled in the art, depending on a target structure.

[Chem. 21]



[0139] Step 1: The reagent for preparing an anion by reacting with (N-I) includes, for example, n-butyllithium, isopropylmagnesium chloride-lithium chloride complex solution, and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, and halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like. The reaction temperature is preferably from -78°C to 50°C, and particularly preferably from -40°C to room temperature.

[0140] Step 2: Dess-Martin periodinane, 2-iodoxybenzoic acid, pyridinium chlorochromate or the like is preferable as the oxidizing agent to be used. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, and halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like. The reaction temperature is preferably from 0°C to 100°C.

[0141] Step 3: The borylation reagent to be used includes bis(pinacolato)diboron and the like, and the tin reagent includes hexamethylditin and the like. Tris(dibenzylideneacetone)dipalladium, palladium acetate, tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst. If necessary, tricyclohexylphosphine, tricyclohexylphosphonium tetrafluoroborate, 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene or the like is used as the ligand. The base to be used for borylation includes potassium acetate and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 70°C to 120°C.

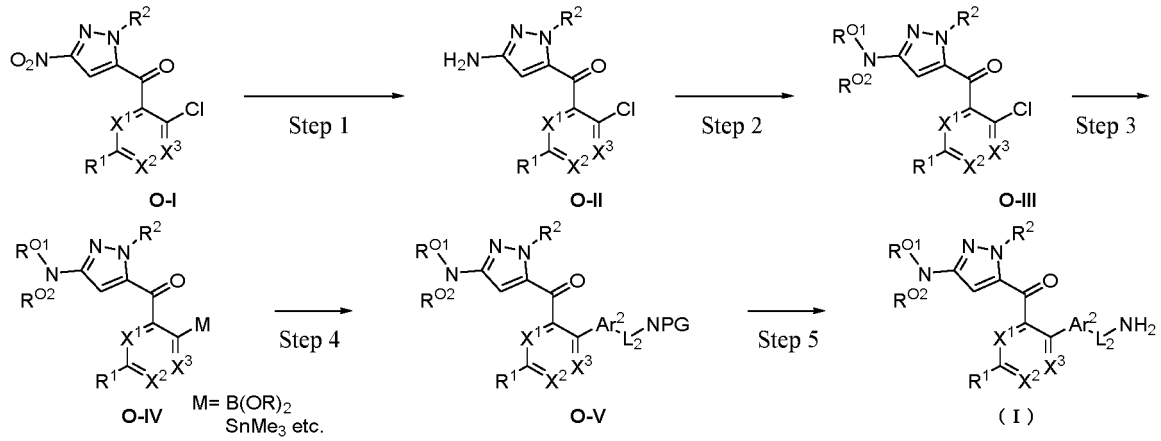
[0142] Step 4: Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst, and the base includes inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 120°C.

[0143] Step 5: As a removal method of the protecting group, a known method widely used in this field can be adopted. For example, when the protecting group is a Boc group, a strong acid such as trifluoroacetic acid, hydrochloric acid or sulfuric acid is preferable, and when the protecting group is phthalimide, hydrazine, ethylenediamine or the like is preferable. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide and the like. The reaction temperature is preferably from 0°C to 100°C.

[0144] When L^1 in the formula (I) is -CO- in the compound of the present invention, the target compound can be synthesized also by utilizing the intermediate pyrazole (O-II) as shown in the following reaction scheme. That is, after the amino group in (O-II) obtained by reducing (O-I) was modified with a reagent having a leaving group to obtain (O-

III), the target compound can be synthesized by the same method as described above.

[Chem. 22]



(Wherein, R^{O1}, R^{O2} are substituents that form $-NR^{O1}R^{O2}$ which may be included in R^3 of formula (I).)

[0145] Step 1: Iron, zinc or the like is preferable as the metal reagent to be used, and the metal reagent is preferably used in combination with a reagent such as ammonium chloride and acetic acid. Preferred solvents include organic solvents such as ethanol, methanol, tetrahydrofuran and the like, mixed solvents obtained by adding water thereto, and the like. The reaction temperature is preferably from room temperature to 100°C.

[0146] Step 2: The reaction reagent having a leaving group includes, for example, alkyl halides, alkyl triflate and the like. Organic bases such as triethylamine, N,N-diisopropylethylamine, and the like and inorganic bases such as potassium carbonate, cesium carbonate and the like are preferable as the base. 1,4-Dioxane, N,N-dimethylformamide, N,N-dimethylacetamide, N-methylpyrrolidone, dimethyl sulfoxide or the like is preferable as the solvent. The reaction temperature is preferably from room temperature to 150°C.

[0147] Step 3: The borylation reagent to be used includes bis(pinacolato)diboron, and the tin reagent includes hexamethylditin and the like. The preferred palladium catalyst includes, for example, tris(dibenzylideneacetone)dipalladium, palladium acetate, tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride and the like. If necessary, tricyclohexylphosphine, tricyclohexylphosphonium tetrafluoroborate, 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene or the like is used as the ligand. The base used for borylation includes, for example, potassium acetate and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 70°C to 120°C.

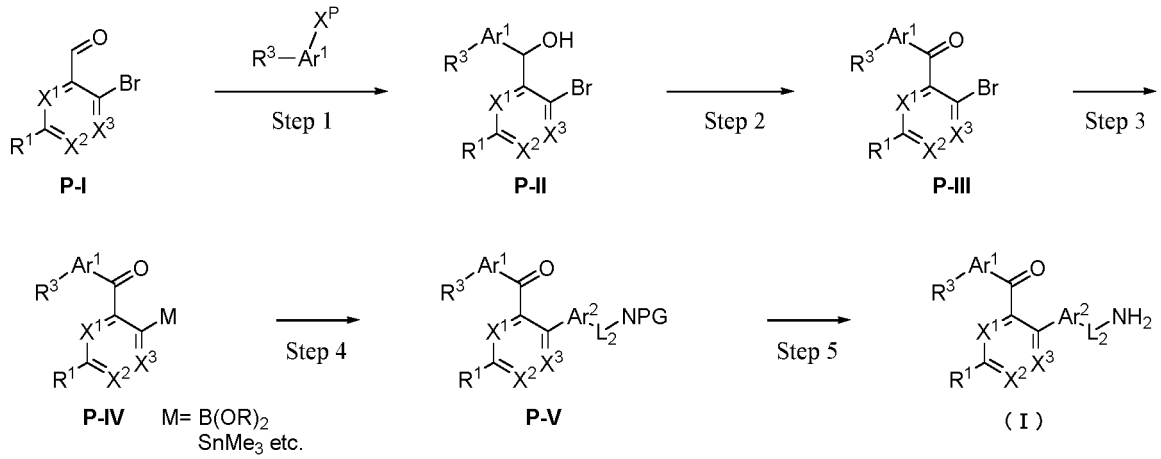
[0148] Step 4: Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst, and the base includes, for example, inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 120°C.

[0149] Step 5: As a removal method of the protecting group, a known method widely used in this field can be adopted. For example, when the protecting group is a Boc group, a strong acid such as trifluoroacetic acid, hydrochloric acid or sulfuric acid is preferable, and when the protecting group is phthalimide, hydrazine, ethylenediamine or the like is preferable. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from 0°C to 100°C.

[0150] When L^1 in the formula (I) is -CO- in the compound of the present invention, as shown in the following reaction

scheme, after reacting the anionic reagent prepared from Ar^1 ring with aldehyde (P-I) to obtain a corresponding alcohol (P-II), the synthesis can be performed by the same method as described above.

[Chem. 23]



(Wherein, X^P is H or a halogen atom.)

[0151] Step 1: The reagent for preparing an anion in the reaction system includes, for example, n-butyllithium, isopropylmagnesium chloride-lithium chloride complex solution and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, and halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like. The reaction temperature is preferably from -78°C to 50°C, and particularly preferably from -40°C to room temperature.

[0152] Step 2: Dess-Martin periodinane, 2-iodoxybenzoic acid, pyridinium chlorochromate or the like is preferable as the oxidizing agent to be used. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, and halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like. The reaction temperature is preferably from 0°C to 100°C.

[0153] Step 3: The borylation reagent to be used includes, for example, bis(pinacolato)diboron, and the tin reagent includes, for example, hexamethylditin, and the like. Tris(dibenzylideneacetone)dipalladium, palladium acetate, tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the preferred palladium catalyst. If necessary, tricyclohexylphosphine, tricyclohexylphosphonium tetrafluoroborate, 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene or the like is used as the ligand. The base to be used for borylation includes, for example, potassium acetate and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 70°C to 120°C.

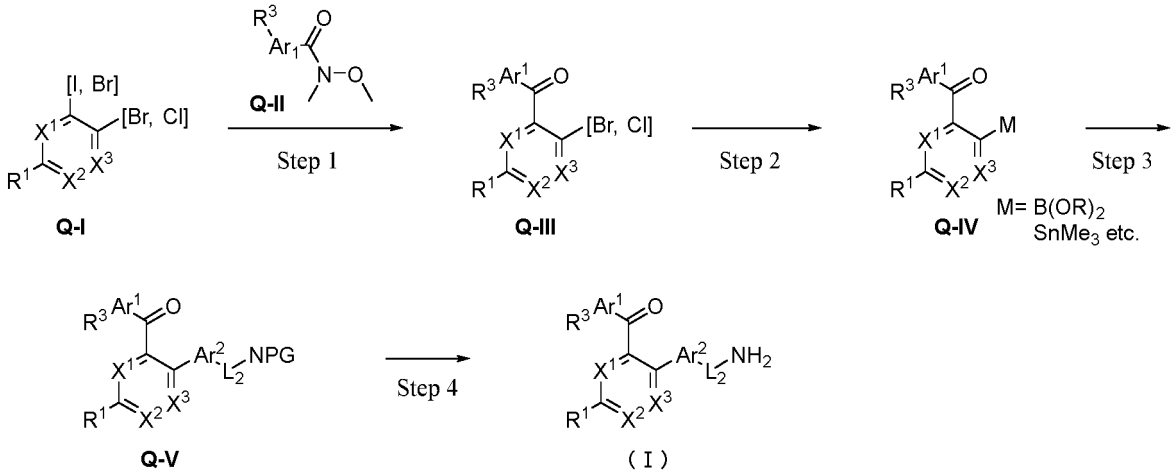
[0154] Step 4: Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst, and the base includes, for example, inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 120°C.

[0155] Step 5: As a removal method of the protecting group, a known method widely used in this field can be adopted. For example, when the protecting group is a Boc group, a strong acid such as trifluoroacetic acid, hydrochloric acid, sulfuric acid, or the like is preferable, and when the protecting group is phthalimide, hydrazine, ethylenediamine or the like is preferable. The solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as

benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from 0°C to 100°C.

[0156] When L^1 in the formula (I) is -CO- in the compound of the present invention, after synthesizing the corresponding ketone (Q-III) using Ar^1 ring having the Weinreb amide (Q-II) as shown in the following reaction scheme, the synthesis can be performed by the same method as described above.

[Chem. 24]



[0157] Step 1: The reagent for preparing an anion in the reaction system includes, for example, n-butyllithium, isopropylmagnesium chloride-lithium chloride complex solution, and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like. The reaction temperature is preferably from -78°C to 50°C, and particularly preferably from -40°C to room temperature.

[0158] Step 2: The borylation reagent to be used includes, for example, bis(pinacolato)diboron, and the tin reagent includes, for example, hexamethylditin and the like. Tris(dibenzylideneacetone)dipalladium, palladium acetate, tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride, or the like is preferable as the palladium catalyst. If necessary, tricyclohexylphosphine, tricyclohexylphosphonium tetrafluoroborate, 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene or the like is used as the ligand. The base to be used for borylation includes, for example, potassium acetate, and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 70°C to 120°C.

[0159] Step 3: Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst, and the base includes, for example, inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 120°C.

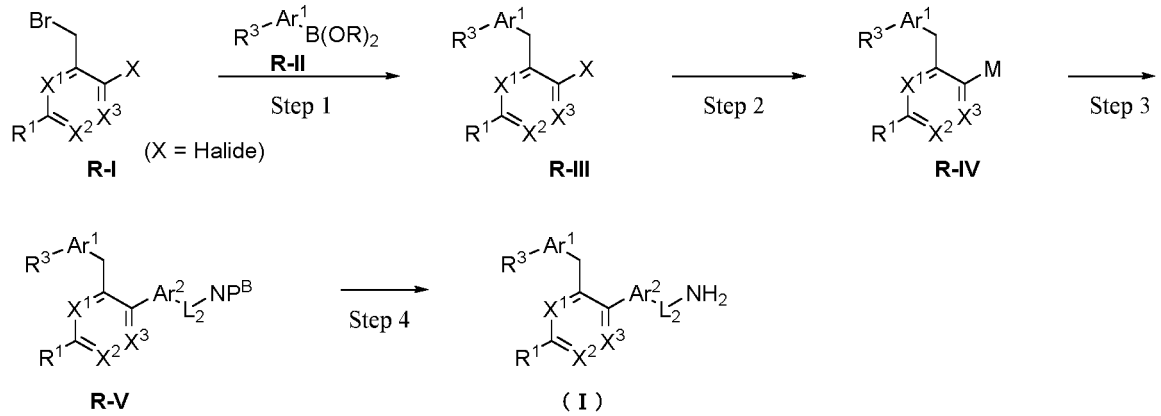
[0160] Step 4: As a removal method of the protecting group, a known method widely used in this field can be adopted. For example, when the protecting group is a Boc group, a strong acid such as trifluoroacetic acid, hydrochloric acid or sulfuric acid is preferable, and when the protecting group is phthalimide, hydrazine, ethylenediamine or the like is preferable. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-

diethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from 0°C to 100°C.

[0161] When L^1 in the formula (I) is $-CH_2-$ in the compound of the present invention, synthesis can be performed by using the following synthesis methods.

[0162] For example, synthesis can be performed as shown in the following reaction scheme. That is, after bonding Ar^1 ring compound (R-II) having a reactive substituent such as a boronic acid derivative with benzyl bromide (R-I) by a cross-coupling reaction, by converting (R-III) to a boron compound, tin compound, or the like, then performing the cross-coupling reaction with the corresponding Ar^2 ring compounds, a biaryl bond can be formed to complete the synthesis. On the other hand, (R-III) can be directly used to perform cross-coupling reaction or the like with Ar^2 ring compounds having suitable reactive substituents without an operation of step 2.

[Chem. 25]



[0163] Step 1: Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst, and the base includes, for example, inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 120°C.

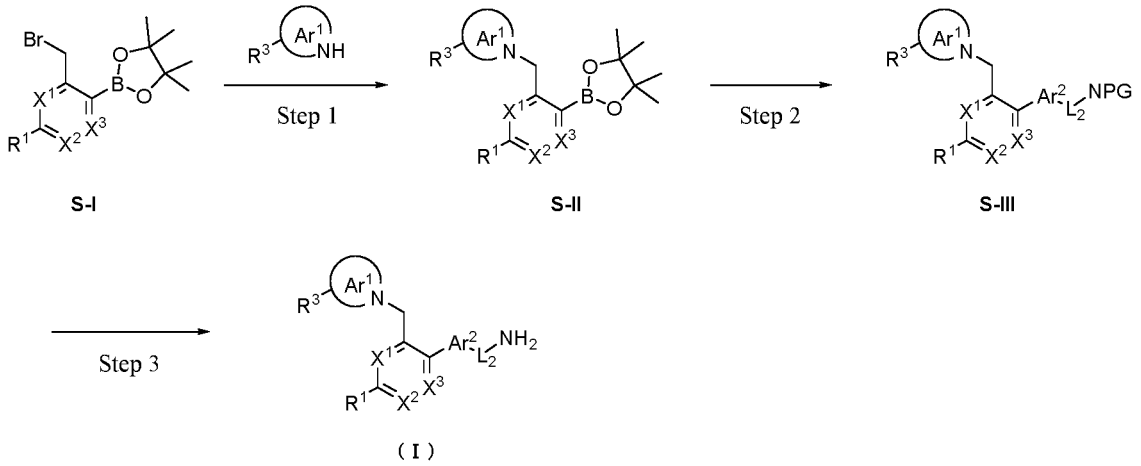
[0164] Step 2: The borylation reagent to be used includes, for example, bis(pinacolato)diboron, and the tin reagent includes, for example, hexamethylditin and the like. Tris(dibenzylideneacetone)dipalladium, palladium acetate, tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride, or the like is preferable as the palladium catalyst. If necessary, tricyclohexylphosphine, tricyclohexylphosphonium tetrafluoroborate, 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene or the like is used as the ligand. The base to be used for borylation includes, for example, potassium acetate and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly from preferably 70°C to 120°C.

[0165] Step 3: Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst, and the base includes, for example, inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water, mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 120°C.

[0166] Step 4: As a removal method of the protecting group, a known method widely used in this field can be adopted. For example, when the protecting group is a Boc group, a strong acid such as trifluoroacetic acid, hydrochloric acid or sulfuric acid is preferable, and when the protecting group is phthalimide, hydrazine or ethylenediamine is preferable. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like, alcohols such as methanol, ethanol, 2-propanol butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from 0°C to 100°C.

[0167] When L^1 in the formula (I) is $-CH_2-$ in the compound of the present invention, as shown in the following reaction scheme, after obtaining (S-II) by bonding to Ar^1 ring through an alkylation reaction using a nitrogen atom in the Ar^1 ring, the synthesis can be performed by the same method as described above.

[Chem. 26]



S-I S-II S-III (I)

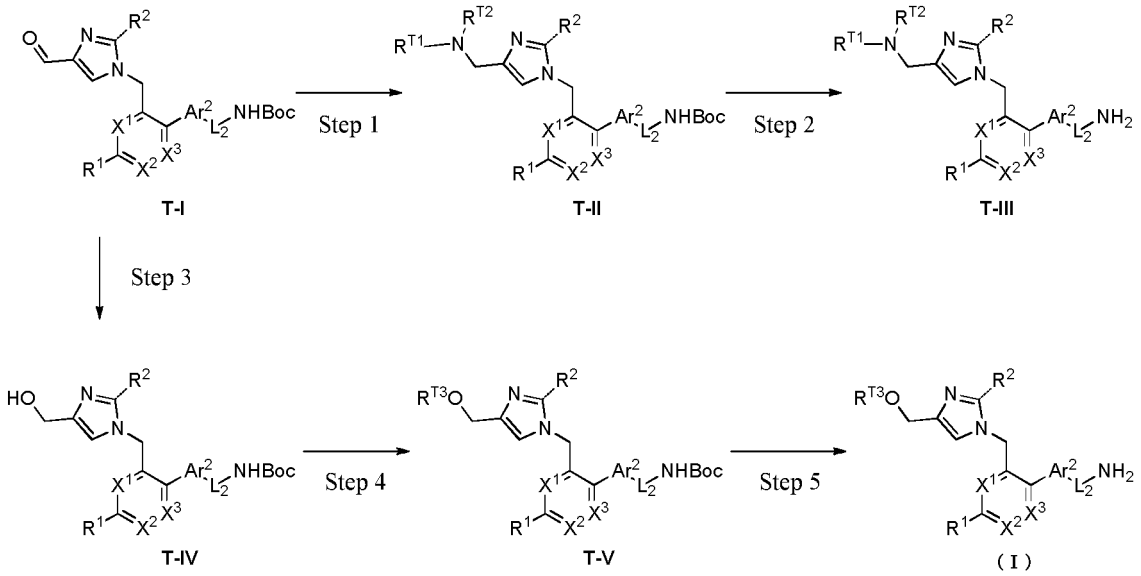
[0168] Step 1: Triethylamine, N,N-diisopropylethylamine, potassium carbonate, cesium carbonate or the like is preferable as the base. Here, the solvent is not particularly limited and includes, for example, ethers such as tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from room temperature to 120°C, and particularly preferably from 40°C to 100°C.

[0169] . Step 2: Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst, and the base includes, for example, inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 120°C.

[0170] Step 3: As a removal method of the protecting group, a known method widely used in this field can be adopted. For example, when the protecting group is a Boc group, a strong acid such as trifluoroacetic acid, hydrochloric acid, sulfuric acid, or the like is preferable, and when the protecting group is phthalimide, hydrazine, ethylenediamine or the like is preferable. Here, the solvent is not particularly limited and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from 0°C to 100°C.

[0171] When L^1 in the formula (I) is $-CH_2-$ in the compound of the present invention, as shown in the following reaction scheme, a target compound in which amino group or alkoxy group is introduced can be synthesized using the aldehyde of intermediate (T-I) as a foothold.

[Chem. 27]



(Wherein, R^{T1}, R^{T2}, R^{T3} are H atoms or C_{1-6} alkyl groups.)

[0172] Step 1: A reductive amination reaction is performed using an amine suitable for the target compound. The imine reducing agent includes, for example, sodium triacetoxyborohydride, sodium cyanoborohydride, and the like. Preferred solvents include, for example, toluene, dichloromethane, dichloroethane, and the like. The reaction temperature is preferably from room temperature to 80°C.

[0173] Step 2: Trifluoroacetic acid, hydrochloric acid, sulfuric acid, or the like, is preferable as the strong acid to be used, and dichloromethane, tetrahydrofuran, ethyl acetate or the like, is preferable as the solvent. The reaction temperature is preferably from 0°C to 50°C, and particularly preferably from 0°C to room temperature.

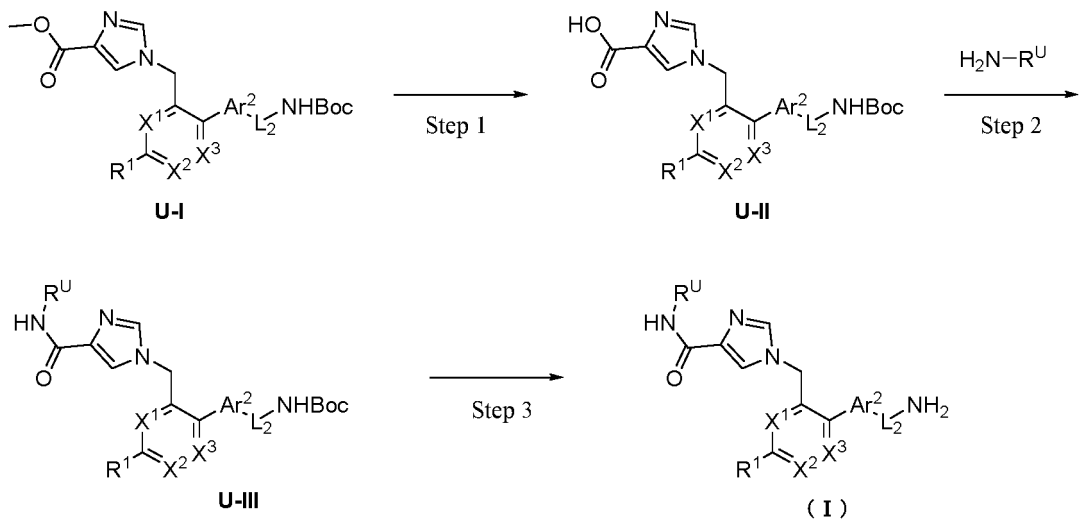
[0174] Step 3: The reducing agent to be used includes, for example, sodium borohydride, lithium borohydride, and the like. Preferred solvents include tetrahydrofuran, methanol, a mixed solvent thereof, and the like. The reaction temperature is preferably from 0°C to room temperature.

[0175] Step 4: Alkyl halide, alkyl triflate or the like is used as a reagent having a leaving group. The base includes, for example, sodium hydride, potassium carbonate, cesium carbonate. Tetrahydrofuran, N,N-dimethylformamide, dimethyl sulfoxide or the like is preferable as the solvent. The reaction temperature is preferably from 0°C to 80°C.

[0176] Step 5: Trifluoroacetic acid, hydrochloric acid, sulfuric acid, or the like is preferable as the strong acid to be used, and dichloromethane, tetrahydrofuran, ethyl acetate or the like is preferable as the solvent. The reaction temperature is preferably from 0°C to 50°C, and particularly preferably from 0°C to room temperature.

[0177] When L^1 in the formula (I) is $-CH_2-$ in the compound of the present invention, as shown in the following reaction scheme, a target compound having an amide group can be synthesized via functional group conversion of the ester group in intermediate (U-I).

[Chem. 28]



(Wherein, R^U is a C_{1-6} alkyl group.)

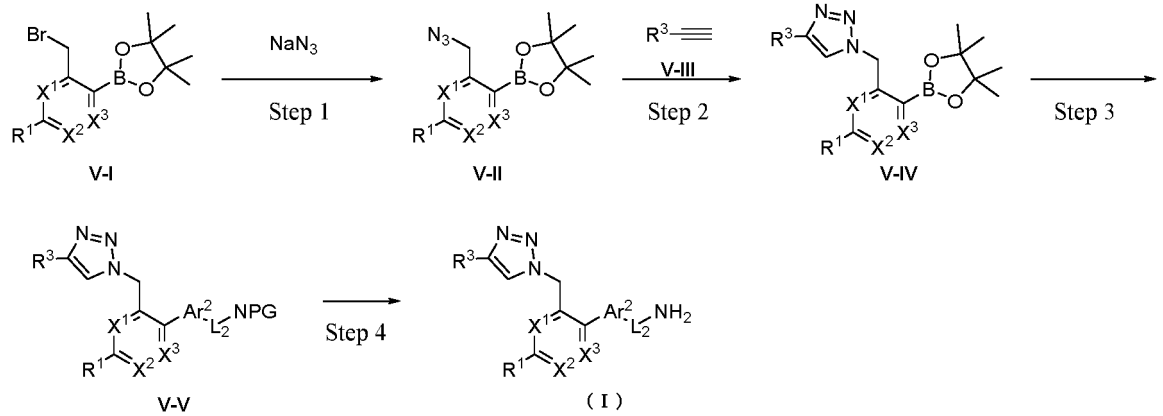
[0178] Step 1: The base includes, for example, inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, and the like, metal alkoxides such as sodium ethoxide, sodium methoxide, and the like, a solution thereof diluted with water, and the like. Here, the solvent is not particularly limited, and includes, for example, tetrahydrofuran, methanol, ethanol, water, a mixed solvent thereof, and the like. The reaction temperature is preferably from 0°C to 60°C.

[0179] Step 2: The condensing agent to be used includes, for example, HATU, HOBt, HOAt, EDCI, and the like. The reaction is performed in the presence of no base or a base such as triethylamine, N,N-diisopropylethylamine, and the like. Tetrahydrofuran, dichloromethane, N,N-dimethylformamide or the like is preferable as the solvent. The reaction temperature is preferably from 0°C to 100°C.

[0180] Step 3: Trifluoroacetic acid, hydrochloric acid, sulfuric acid, or the like is preferable as the strong acid to be used, and a solvent such as dichloromethane, tetrahydrofuran, ethyl acetate or the like is preferable as the solvent. The reaction temperature is preferably from 0°C to 50°C, and particularly preferably from 0°C to room temperature.

[0181] When L^1 in the formula (I) is $-CH_2-$ in the compound of the present invention, the synthesis can also be performed by the method shown in the following reaction scheme. That is, after obtaining triazole (V-IV) by reacting the acetylene compound (V-III) with the (V-II) into which an azide group is introduced, the synthesis can be performed by the same method as described above.

[Chem. 29]



[0182] Step 1: This reaction is a reaction of introducing an azido group using sodium azide. The solvent includes, for example, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from room temperature to 100°C.

[0183] Step 2: This reaction is a reaction of performing triazole ring synthesis using an alkyne compound corresponding to the target compound. Copper(I) iodide, copper(I) bromide or the like is preferable as the metal reagent, and if necessary,

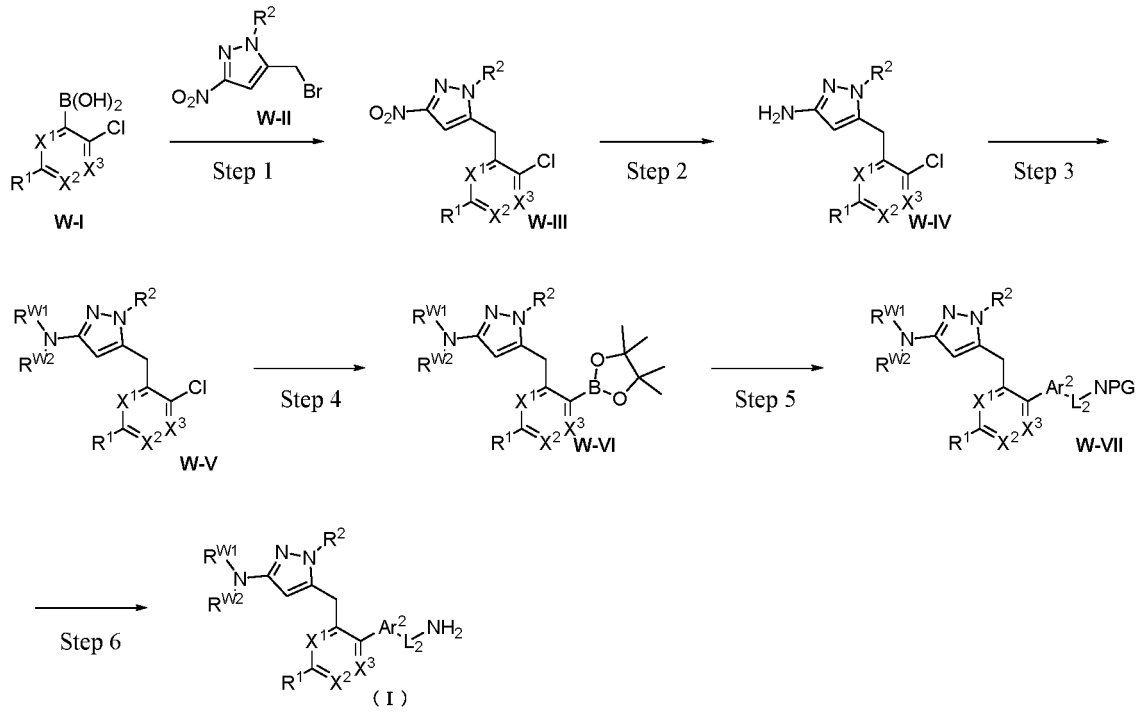
a ligand such as tris[(1-benzyl-1H-1,2,3-triazol-4-yl)methyl]amine (TBTA) is also added. Here, the solvent is not particularly limited, and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from room temperature to 80°C.

[0184] Step 3: Preferred palladium catalyst includes, for example, tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride, and the like, and the base includes, for example, inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like. Here, the solvent is not particularly limited, and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 120°C.

[0185] Step 4: As a removal method of the protecting group, a known method widely used in this field can be adopted. For example, when the protecting group is a Boc group, a strong acid such as trifluoroacetic acid, hydrochloric acid, sulfuric acid, or the like is preferable, and when the protecting group is phthalimide, hydrazine, ethylenediamine or the like is preferable. The solvent is not particularly limited, and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from 0°C to 100°C.

[0186] When L^1 in the formula (I) is $-CH_2-$ in the compound of the present invention, the synthesis can be performed also by the method shown in the following reaction scheme. That is, after obtaining (W-V) by a coupling reaction between boronic acid (W-I) and nitropyrazole ring (W-II), reducing a nitro group, and modifying an amino group, the target compound can be synthesized by the same method as described above.

[Chem. 30]



(Wherein, R^{W1} and R^{W2} are substituents which form $-NR^{W1}R^{W2}$ which may be included in R^3 of the formula (I).)

[0187] Step 1: Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenyl-

phosphino)ferrocene]palladium dichloride, or the like is preferable as the palladium catalyst and the base includes, for example, inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like. Here, the solvent is not particularly limited, and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 120°C.

[0188] Step 2: Iron, zinc, or the like is preferable as the metal reagent to be used, and is preferably used in combination with a reagent such as ammonium chloride, acetic acid, and the like. Preferred solvents include, for example, organic solvents such as ethanol, methanol and tetrahydrofuran, and mixed solvents obtained by adding water thereto, and the like. The reaction temperature is preferably from room temperature to 100°C.

[0189] Step 3: The reaction reagent having a leaving group includes, for example, alkyl halides, alkyl triflate, and the like. Organic bases such as triethylamine, N,N-diisopropylethylamine, or the like, or inorganic bases such as potassium carbonate, cesium carbonate, or the like is preferable as the base. 1,4-Dioxane, N,N-dimethylformamide, N,N-dimethylacetamide, N-methylpyrrolidone, dimethyl sulfoxide or the like is preferable as the solvent. The reaction temperature is preferably from room temperature to 150°C.

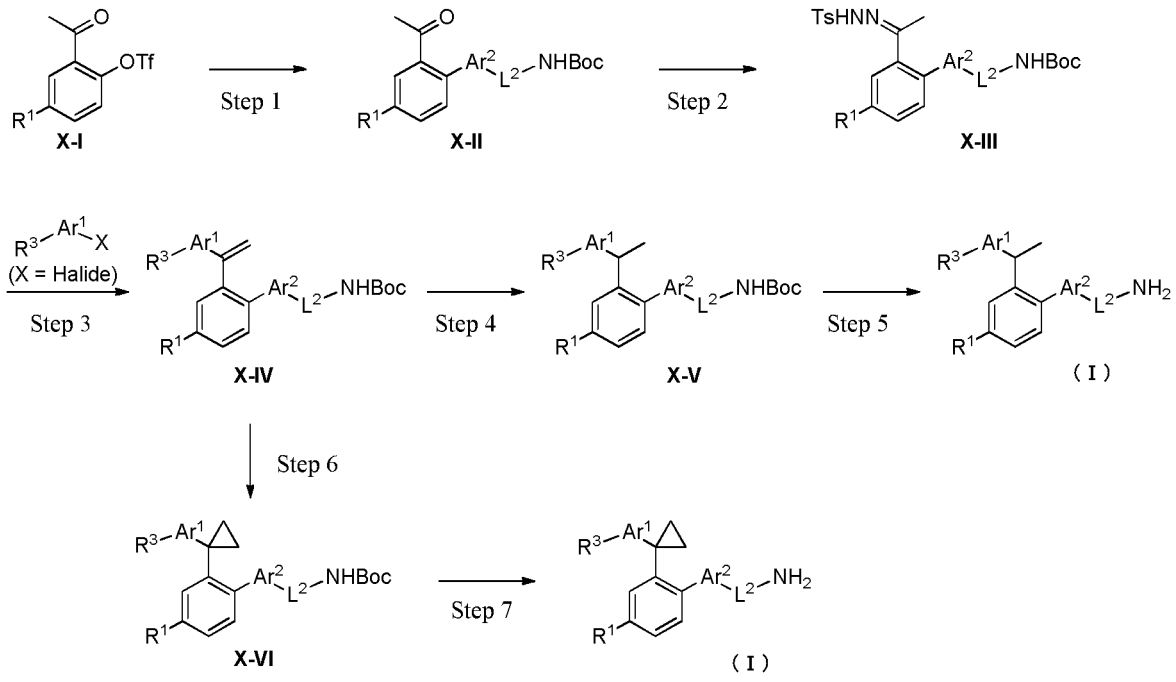
[0190] Step 4: The borylation reagent includes, for example, bis(pinacolato)diboron, and the like. Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride, tris(dibenzylideneacetone)dipalladium, palladium acetate, XPhos-Pd-G2, or the like is preferable as the catalyst. If necessary, the ligand such as tricyclohexylphosphine, 2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl, 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl, or the like can be used. Potassium acetate or the like is preferable as the base. Preferred solvents include, for example, 1,4-dioxane, dimethyl sulfoxide, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 70°C to 120°C.

[0191] Step 5: Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride, or the like is preferable as the palladium catalyst, and the base includes, for example, inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like. Here, the solvent is not particularly limited, and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 120°C.

[0192] Step 6: As a removal method of the protecting group, a known method widely used in this field can be adopted. For example, when the protecting group is a Boc group, a strong acid such as trifluoroacetic acid, hydrochloric acid, sulfuric acid, or the like is preferable, and when the protecting group is phthalimide, hydrazine, ethylenediamine or the like is preferable. Here, the solvent is not particularly limited, and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from 0°C to 100°C.

[0193] When L^1 in the formula (I) is -CHMe-, -C(=CH_2)-, or a 1,1-cyclopropylidene group in the compound of the present invention, synthesis can be performed as shown in the following reaction scheme. That is, after reacting tosylhydrazone (X-III) with an Ar^1 ring compound having a halogen atom to obtain an exoolefin (X-IV), the target compound can be synthesized by reducing or cyclopropanating the olefin, and then deprotecting. The compound represented by formula (I) in which L^1 is -C(=CH_2)- can be synthesized by deprotecting (X-IV).

[Chem. 31]



[0194] Step 1: Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride, or the like is preferable as the palladium catalyst, and the base includes, for example, inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like. Here, the solvent is not particularly limited, and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 120°C.

[0195] Step 2: This reaction is a reaction of forming tosylhydrazone using tosylhydrazine as a reagent. Preferred solvents include toluene, methanol, ethanol, and the like. The reaction temperature is preferably from room temperature to 120°C.

[0196] Step 3: This reaction is a reaction of synthesizing an exoolefin by performing a coupling reaction between tosylhydrazone and aryl halide. Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride, tris(dibenzylideneacetone)dipalladium, palladium acetate, or the like is preferable as the catalyst. If necessary, a ligand such as 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene, 2-(dicyclohexylphosphino)-2',4',6'-tri-isopropyl-1,1'-biphenyl, 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl, or the like can be used. Preferred bases include cesium carbonate, lithium tert-butoxide, tripotassium phosphate. Preferred solvents include 1,4-dioxane, toluene, fluorobenzene, and the like. The reaction temperature is preferably from 50°C to 150°C.

[0197] Step 4: This reaction is a reaction of reducing an olefin by combining a metal reagent such as palladium carbon (Pd/C) and a hydrogen source such as hydrogen gas. Ethanol, methanol, ethyl acetate or the like is preferable as the solvent. The reaction temperature is preferably from 0°C to 100°C.

[0198] Step 5: Trifluoroacetic acid, hydrochloric acid, sulfuric acid, or the like is preferable as the strong acid to be used, and dichloromethane, tetrahydrofuran, ethyl acetate or the like is preferable as the solvent. The reaction temperature is preferably from 0°C to 50°C, and particularly preferably from 0°C to room temperature.

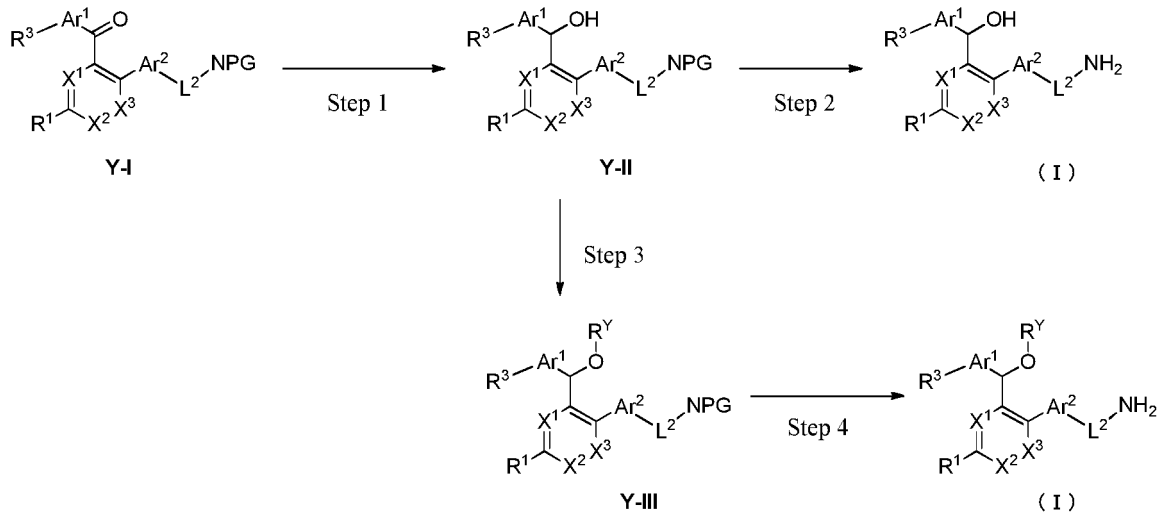
[0199] Step 6: This reaction is a reaction of converting an olefin to cyclopropane using trimethylsulfoxonium iodide. Preferred bases include, for example, sodium hydride, potassium tert-butoxide, and the like. Dimethyl sulfoxide, tetrahydrofuran or the like is preferable as the solvent. The reaction temperature is preferably from 0°C to 100°C.

[0200] Step 7: Trifluoroacetic acid, hydrochloric acid, sulfuric acid, or the like is preferable as the strong acid to be used, and dichloromethane, tetrahydrofuran, ethyl acetate, or the like is preferable as the solvent. The reaction temperature is preferably from 0°C to 50°C, and particularly preferably from 0°C to room temperature.

[0201] When L^1 in the formula (I) is -CH(R^{11})- in the compound of the present invention, synthesis can be performed by using the following methods.

[0202] For example, synthesis can be performed as shown in the following reaction scheme. That is, after reducing the ketone of (Y-I) prepared by the synthesis method described above, the target compound can be synthesized by deprotecting the amino group. It is also possible to modify the hydroxy group in intermediate (Y-II) by an alkylation reaction or the like.

[Chem. 32]



(Wherein, R^Y is a substituent which forms -OR^Y which satisfies R^{11} in the formula (I).)

[0203] Step 1: The reducing reagent includes, for example, sodium borohydride, lithium borohydride, and the like. Preferred solvents include, for example, tetrahydrofuran, methanol, ethanol, a mixed solvent thereof, and the like. The reaction temperature is preferably from 0°C to 50°C.

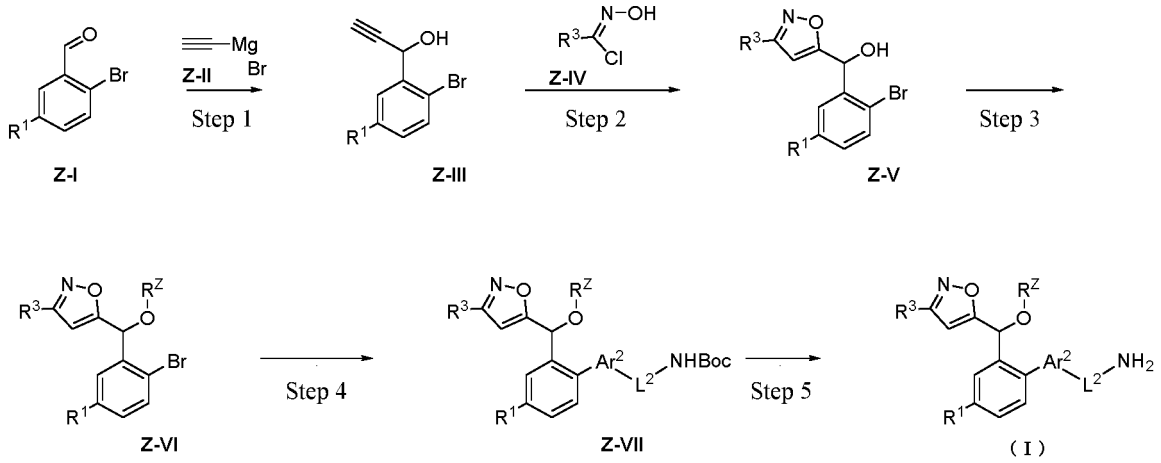
[0204] Step 2: As a removal method of the protecting group, a known method widely used in this field can be adopted. For example, when the protecting group is a Boc group, a strong acid such as trifluoroacetic acid, hydrochloric acid, sulfuric acid, or the like is preferable, and when the protecting group is phthalimide, hydrazine, ethylenediamine or the like is preferable. Here, the solvent is not particularly limited, and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from 0°C to 100°C.

[0205] Step 3: Alkyl halide, alkyl triflate or the like is used as the reagent having a leaving group. The base includes, for example, sodium hydride, potassium carbonate, cesium carbonate, and the like. Tetrahydrofuran, N,N-dimethylformamide, dimethyl sulfoxide, or the like is preferable as the solvent. The reaction temperature is preferably from 0°C to 80°C.

[0206] Step 4: As a removal method of the protecting group, a known method widely used in this field can be adopted. For example, when the protecting group is a Boc group, a strong acid such as trifluoroacetic acid, hydrochloric acid, sulfuric acid, or the like is preferable, and when the protecting group is phthalimide, hydrazine, ethylenediamine or the like is preferable. Here, the solvent is not particularly limited, and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from 0°C to 100°C.

[0207] When L^1 in the formula (I) is -CH(R^{11})- in the compound of the present invention, the synthesis can be performed also as shown in the following reaction scheme. That is, after introducing an ethynyl group on the raw material aldehyde (Z-I), cyclization reaction is performed using (Z-IV) to obtain target isoxazole (Z-V) having R^3 substituent. After modifying the hydroxy group of (Z-V) by an alkylation reaction or the like, the target compound can be synthesized by deprotecting the amino group.

[Chem. 33]



(Wherein, R^Z is a substituent which forms $-OR^Z$ which satisfies R^{11} in the formula (I).)

[0208] Step 1: This reaction is an addition reaction of ethynylmagnesium bromide (Z-II) to aldehyde (Z-I). Tetrahydrofuran, dichloromethane, or the like is preferable as the solvent to be used. The reaction temperature is preferably from -78°C to room temperature.

[0209] Step 2: This reaction is a reaction of constructing an isoxazole ring using an oxime reagent (Z-IV) corresponding to the target compound. Potassium carbonate, sodium carbonate, cesium carbonate, or the like is preferable as the base, and 1,4-dioxane, toluene, or the like is preferable as the solvent. The reaction temperature is preferably from 50°C to 120°C.

[0210] Step 3: Alkyl halide, alkyl triflate or the like is used as the reagent having a leaving group. The base includes, for example, sodium hydride, potassium carbonate, cesium carbonate, and the like. Tetrahydrofuran, N,N-dimethylformamide, dimethyl sulfoxide or the like is preferable as the solvent. The reaction temperature is preferably from 0°C to 80°C.

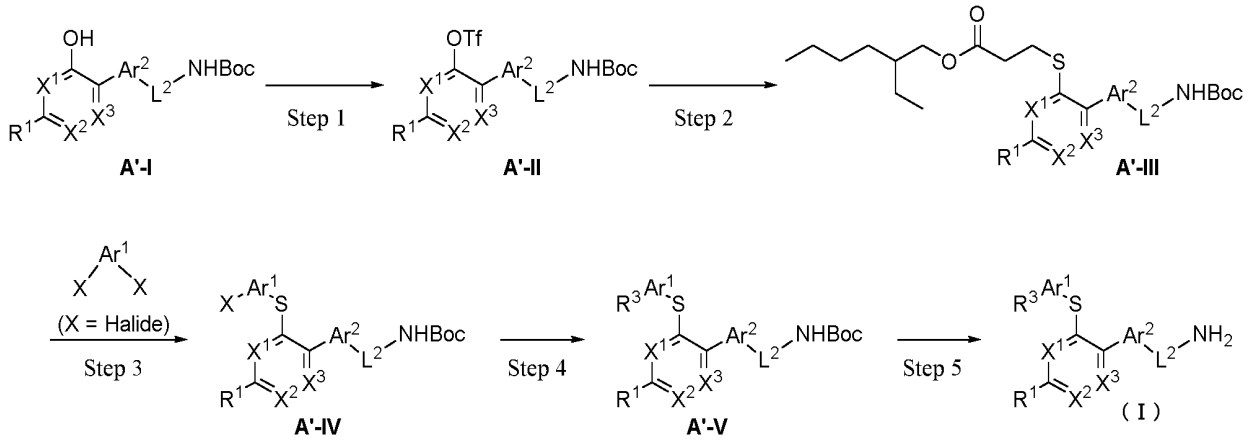
[0211] Step 4: Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst, and the base includes, for example, inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like. Here, the solvent is not particularly limited, and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water, a mixed solvent thereof, and the like. The reaction temperature is preferably from 50°C to 150°C, and particularly preferably from 80°C to 120°C.

[0212] Step 5: Trifluoroacetic acid, hydrochloric acid, sulfuric acid, or the like is preferable as the strong acid to be used, and dichloromethane, tetrahydrofuran, ethyl acetate or the like is preferable as the solvent. The reaction temperature is preferably from 0°C to 50°C, and particularly preferably from 0°C to room temperature.

[0213] When L^1 in the formula (I) is -S- or -SO- in the compound of the present invention, the synthesis can be performed using the following methods.

[0214] For example, synthesis can be performed as shown in the following reaction scheme. That is, after converting the intermediate (A'-I) obtained by the above-mentioned synthesis method into triflate (A'-II), a thiol side chain is introduced by a coupling reaction, and this compound (A'-III) is treated with a suitable base and subjected to an aromatic nucleophilic substitution reaction to be bonded with Ar^1 ring. If necessary, after this, the target compound can be synthesized by introducing the target side chain substituent using a halogen atom in Ar^1 as a foothold. If the Ar^1 compound used in step 3 has already been modified with R^3, the operation in step 4 can be omitted.

[Chem. 34]



[0215] Step 1: The triflation agent to be used include trifluoromethanesulfonic anhydride (TfzO), and the like and pyridine, triethylamine, N,N-diisopropylethylamine or the like is preferable as the base. Preferred solvents include, for example, tetrahydrofuran, dichloromethane, 1,2-dichloroethane, and the like. The reaction temperature is preferably from -20°C to 50°C.

[0216] Step 2: Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride, tris(dibenzylideneacetone)dipalladium, palladium acetate, or the like is preferable as the catalyst. If necessary, the ligand such as 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene, 2-(dicyclohexylphosphino)-2',4',6'-tri-isopropyl-1,1'-biphenyl and 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl, or the like can be used. Preferred bases include, for example, N,N-diisopropylethylamine, triethylamine, potassium carbonate, cesium carbonate, and the like. The solvent includes, for example, 1,4-dioxane, tetrahydrofuran, N,N-dimethylformamide, and the like. The reaction temperature is preferably from 50°C to 150°C.

[0217] Step 3: Potassium carbonate, cesium carbonate, 1,8-diazabicyclo[5.4.0]-7-undecene (DBU) or the like is preferable as the base. Preferred solvents include, for example, 1,4-dioxane, tetrahydrofuran, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from 0°C to 150°C.

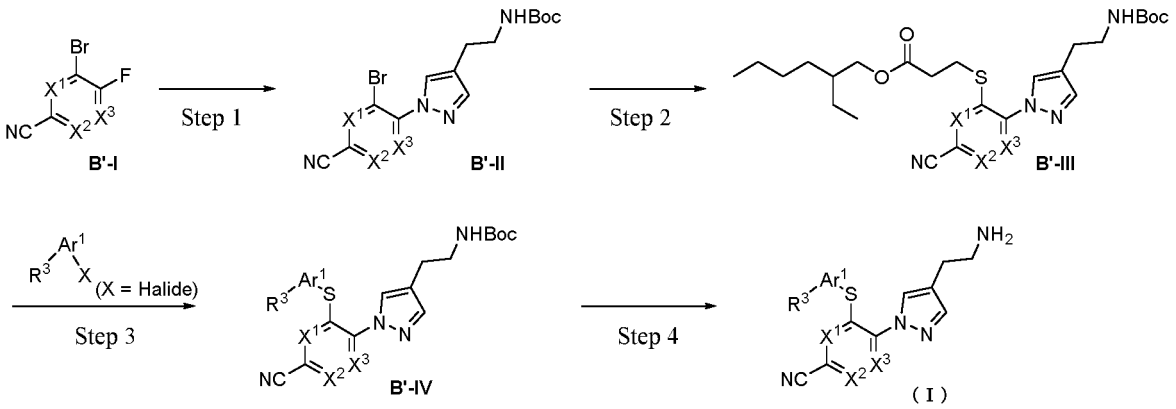
[0218] Step 4: For introduction of the R^3 substituent, a known method commonly used in the art can be adopted. For example, when the R^3 substituent is introduced using boronic acid derivatives, tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride or the like is preferable as the palladium catalyst, and the base includes, for example, inorganic salts such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, tripotassium phosphate, and the like. Here, the solvent is not particularly limited, and includes, for example, aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, alcohols such as methanol, ethanol, 2-propanol, butanol, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, water, mixed solvent thereof, and the like. The reaction temperature is preferably form 50°C to 150°C, and particularly preferably from 80°C to 120°C.

[0219] Further, for example, when an alcohol or an amine corresponding to the R^3 substituent is reacted, preferred bases include, for example, organic bases such as triethylamine, N,N-diisopropylethylamine, and the like, and inorganic bases such as potassium carbonate, cesium carbonate, and the like. Here, the solvent is not particularly limited, and includes, for example, ethers such as tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and the like, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from room temperature to 150°C.

[0220] Step 5: Trifluoroacetic acid, hydrochloric acid, sulfuric acid, or the like is preferable as the strong acid to be used, and dichloromethane, tetrahydrofuran, ethyl acetate or the like is preferable as the solvent. The reaction temperature is preferably from 0°C to 50°C, and particularly preferably 0°C to room temperature.

[0221] When L^1 in the formula (I) is -S- in the compound of the present invention, synthesis can be performed also as shown in the following reaction scheme. That is, since an aromatic nucleophilic substitution reaction can be used as a method for bonding with an Ar^2 ring such as pyrazole or the like, after the formation of a biaryl bond, the synthesis can be performed in the same manner as in the above scheme.

[Chem. 35]



[0222] Step 1: Triethylamine, N,N-diisopropylethylamine, potassium carbonate, cesium carbonate, or the like is preferable as the base to be used. Preferred solvents include, for example, 1,4-dioxane, tetrahydrofuran, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from room temperature to 150°C.

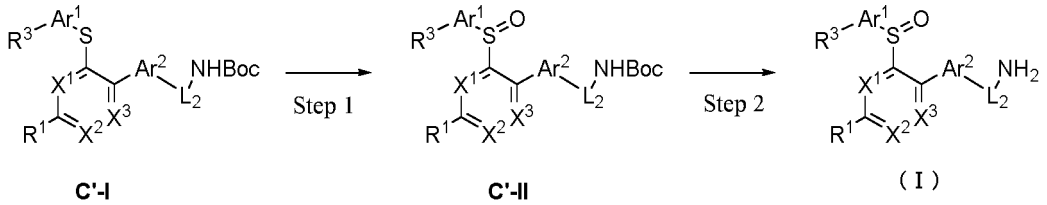
[0223] Step 2: Tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium dichloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride, tris(dibenzylideneacetone)dipalladium, palladium acetate, or the like is preferable as the catalyst. If necessary, the ligand such as 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene, 2-(dicyclohexylphosphino)-2',4',6'-tri-isopropyl-1,1'-biphenyl, 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl, or the like can be used. Preferred bases include N,N-diisopropylethylamine, triethylamine, potassium carbonate, cesium carbonate, and the like. The solvent includes, for example, 1,4-dioxane, tetrahydrofuran, N,N-dimethylformamide, and the like. The reaction temperature is preferably from 50°C to 150°C.

[0224] Step 3: Potassium carbonate, cesium carbonate, 1,8-diazabicyclo[5.4.0]-7-undecene (DBU) or the like is preferable as the base. Preferred solvents include, for example, 1,4-dioxane, tetrahydrofuran, N,N-dimethylformamide, N-methylpyrrolidone, dimethyl sulfoxide, and the like. The reaction temperature is preferably from 0°C to 150°C.

[0225] Step 4: Trifluoroacetic acid, hydrochloric acid, sulfuric acid, or the like is preferable as the strong acid to be used, and dichloromethane, tetrahydrofuran, ethyl acetate or the like is preferable as the solvent. The reaction temperature is preferably from 0°C to 50°C, and particularly preferably from 0°C to room temperature.

[0226] When L^1 in the formula (I) is -SO- in the compound of the present invention, as shown in the following reaction scheme, the target compound can be synthesized by oxidizing sulfide (C'-I) to convert to sulfoxide (C'-II), and then performing deprotection.

[Chem. 36]



[0227] Step 1: The oxidizing agent to be used includes, for example, 3-chloroperbenzoic acid and the like. The solvent includes, for example, 1,4-dioxane, tetrahydrofuran, N,N-dimethylformamide, dimethyl sulfoxide, and the like. The reaction temperature is preferably from 0°C to 100°C.

[0228] Step 2: Trifluoroacetic acid, hydrochloric acid, sulfuric acid, or the like is preferable as the strong acid to be used, and dichloromethane, tetrahydrofuran, ethyl acetate, or the like is preferable as the solvent. The reaction temperature is preferably from 0°C to 50°C, and particularly preferably from 0°C to room temperature.

[0229] Pharmaceutically acceptable salts of the compounds represented by formula (I) are not particularly limited as long as they are pharmaceutically acceptable salts, and include, for example, salts with inorganic acids such as hydrogen chloride, hydrogen bromide, sulfuric acid, nitric acid, phosphoric acid, carbonic acid, and the like, salts with organic acids

such as maleic acid, fumaric acid, citric acid, malic acid, tartaric acid, lactic acid, succinic acid, benzoic acid, oxalic acid, methanesulfonic acid, benzenesulfonic acid, p-toluenesulfonic acid, acetic acid, trifluoroacetic acid, formic acid, and the like, salts with amino acids such as glycine, lysine, arginine, histidine, ornithine, glutamic acid, aspartic acid, and the like, salts with alkali metals such as sodium, potassium, lithium, and the like, salts with alkaline earth metals such as calcium, magnesium, and the like, salts with metals such as aluminum, zinc, iron, and the like, salts with organic oniums such as tetramethylammonium, choline, and the like, and salts with organic bases such as ammonia, propanediamine, pyrrolidine, piperidine, pyridine, ethanolamine, N,N-dimethylethanolamine, 4-hydroxypiperidine, t-octylamine, dibenzylamine, morpholine, glucosamine, phenylglycyl alkyl ester, ethylenediamine, N-methylglucamine, guanidine, diethylamine, triethylamine, dicyclohexylamine, N,N'-dibenzylethylenediamine, chloroprocaine, procaine, diethanolamine, N-benzylphenylamine, piperazine, tris(hydroxymethyl)aminomethane, and the like.

[0230] Further, the compounds represented by formula (I) or pharmaceutically acceptable salts thereof include various hydrates and solvates. The solvents of the solvates include, though not particularly limited, for example, methanol, ethanol, 1-propanol, 2-propanol, butanol, t-butanol, acetonitrile, acetone, methyl ethyl ketone, chloroform, ethyl acetate, diethyl ether, t-butylmethyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, 1,2-diethoxyethane, benzene, toluene, N,N-dimethylformamide, dimethyl sulfoxide, and the like.

[0231] The medically acceptable salts of the compound represented by the formula (I) may be appropriately produced based on conventional knowledge in the art.

[0232] The compounds represented by formula (I) or pharmaceutically acceptable salts thereof include stereoisomers, racemates and all possible optically active substances thereof.

[0233] The compound represented by formula (I) of the present invention or the pharmaceutically acceptable salt thereof can be used in any formulation such as solid preparation, semi-solid preparation and liquid preparation, or any application such as oral and non-oral preparations (injections, percutaneous absorption agents, eye drops, suppositories, transnasal absorption agents, inhalants, and the like).

[0234] The pharmaceutical composition containing a compound represented by formula (I) of the present invention or a pharmaceutically acceptable salt thereof is prepared using additives usually used for formulation. The additives for a solid preparation includes, for example, an excipient such as lactose, saccharose, glucose, corn starch, potatostarch, crystalline cellulose, light anhydrous silicic acid, synthetic aluminum silicate, magnesium aluminometasilicate, calcium hydrogen phosphate, and the like, a binder such as crystalline cellulose, carboxymethyl cellulose, hydroxypropyl cellulose, carboxymethylcellulose sodium, polyvinyl pyrrolidone, and the like, a disintegrating agent such as starch, carboxymethylcellulose sodium, carboxymethylcellulose calcium, croscarmellose sodium and sodium carboxy methyl starch, and the like, a lubricant such as talc, stearic acids, and the like, a coating agent such as hydroxymethylpropylcellulose, hydroxypropylmethylcellulose phthalate, ethylcellulose, and the like, and a coloring agent; the additives for a semisolid preparation include, for example, a substrate such as white petrolatum and the like; and the additives for a liquid preparation includes, for example, a solvent such as ethanol, and the like, a solubilizing agent such as ethanol, and the like, a preservative such as para-hydroxybenzoate, and the like, a isotonizing agent such as glucose, and the like, a buffer such as citric acid, and the like, an antioxidant such as L-ascorbic acid, and the like, a chelating agent such as EDTA, and the like, and a suspending agent and an emulsifying agent such as polysorbate 80 and the like.

[0235] The therapeutically effective amount of the active ingredient in the therapeutic agent or prophylactic agent in the present invention, which depends on the route of administration, the age and sex of the patient, and the severity of the disease, is usually of the order of 0.1 to 1000 mg/day, and the frequency of administration is usually one to three times/day to one to seven times/week. The preparation is preferably prepared so as to satisfy such conditions.

[0236] In the present invention, the term "prevention" means to prevent incidence or onset of diseases in an individual who is not affected by diseases or has not yet developed diseases and the term "treatment" means to cure, suppress, or remedy diseases or symptoms in an individual who has already been affected by diseases or has developed diseases.

[Examples]

[0237] Hereinafter, the present invention will be described in greater detail by way of working examples, but not limited thereto. Abbreviations in the present invention are as follows:

BINAP = 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
DBU = 1,8-diazabicyclo[5.4.0]-7-undecene
DMA = N,N-dimethylacetamide
DMF = N,N-dimethylformamide
DMSO = dimethyl sulfoxide
HATU = 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxide hexafluorophosphate
NMP = 1-methyl-2-pyrrolidone
TFA = trifluoroacetic acid

THF = tetrahydrofuran

[0238] The structure of the novel compound isolated was identified by ^{1}H-NMR and/or mass spectrometry using a single quadrupole instrumentation equipped with an electron spray source, or by other suitable analytical methods.

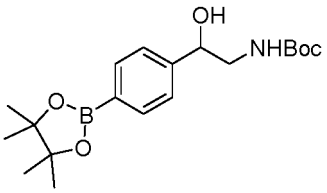
[0239] For the measurement of ^{1}H-NMR spectrum (400 MHz, DMSO-d_6, $CDCl_3$, or CD_3OD), the chemical shift (δ: ppm) and coupling constant (J: Hz) are shown. As for the result of mass spectrometry, the measured value observed as M^++H, that is, the value obtained by adding the mass of a proton (H^+) to the molecular mass of a compound (M) is shown. The abbreviations used are as follows:
s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, brs = broad singlet, m = multiplet.

[Reference Example 1]

tert-Butyl (2-hydroxy-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaboran-2-yl)phenyl)ethyl)carbamate

[0240]

[Chem. 37]



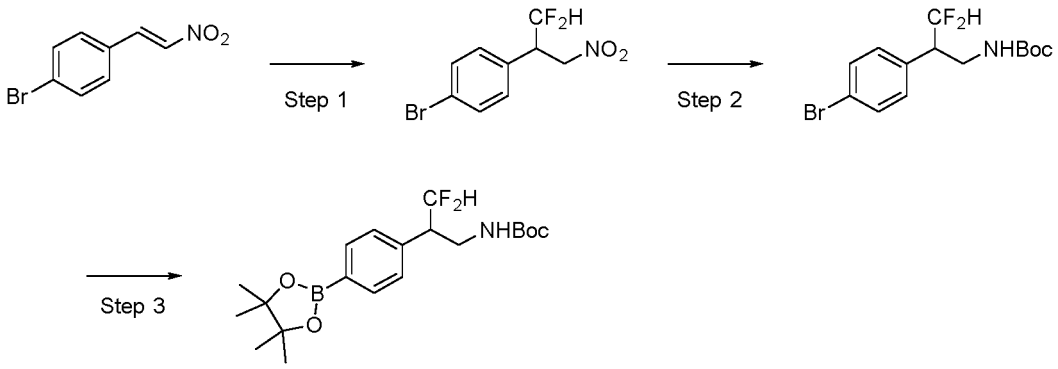
[0241] tert-Butyl (2-(4-bromophenyl)-2-hydroxyethyl)carbamate (503 mg, 1.59 mmol) was dissolved in 1,4-dioxane (10 mL), then to the solution, bis(pinacolato)diboron (404 mg, 1.59 mmol), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium (61 mg, 0.084 mmol) and potassium acetate (469 mg, 4.78 mmol) were added, and the mixture was stirred at 90°C for 15 hours. The reaction mixture was cooled to room temperature, filtered through Celite, and then concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the title compound (412 mg, 71%).
^{1}H-NMR ($CDCl_3$) δ: 7.81 (2H, d, J = 7.8 Hz), 7.38 (2H, d, J = 7.8 Hz), 4.90-4.86 (2H, m), 3.53-3.45 (1H, m)), 3.27-3.20 (1H, m), 1.45 (9H, s), 1.34 (12H, s).

[Reference Example 2]

tert-Butyl N-[3,3-difluoro-2-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]propyl]carbamate

[0242]

[Chem. 38]



Step 1: 1-Bromo-4-(1,1-difluoro-3-nitropropan-2-yl)benzene

[0243] 1-Bromo-4-[(E)-2-nitroethenyl]benzene (1 g) was dissolved in acetonitrile (4.4 mL), the solution was cooled to 0°C, then to the solution, (bromodifluoromethyl)trimethylsilane (1.03 mL), triphenylphosphine (1.38 g), and 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone (1.06 mL) were added, and the mixture was stirred at room temperature for 30 minutes. The reaction mixture was cooled to - 20°C, then to the mixture, chlorotrimethylsilane (0.11 mL) and methanol (0.89 mL) were added, and the mixture was stirred at the same temperature for 15 minutes and then heated to room temperature. Water (4 mL) and pyridine (0.42 mL) were added to the reaction mixture, and the mixture was stirred at 80°C for 1.5 hours, and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (785 mg).
^{1}H-NMR ($CDCl_3$) δ: 7.54 (2H, d, J = 9.0 Hz), 7.18 (2H, d, J = 8.2 Hz), 6.01 (1H, td, J = 55.3, 2.7 Hz), 4.94 (1H, dd, J = 13.7, 5.5 Hz), 4.83 (1H, ddd, J = 71.4, 13.7, 7.3 Hz), 4.06-3.93 (1H, m).

Step 2: tert-Butyl N-[2-(4-bromophenyl)-3,3-difluoropropyl]carbamate

[0244] 1-Bromo-4-(1,1-difluoro-3-nitropropan-2-yl)benzene (785 mg) was suspended in a mixed solvent of ethanol (7 mL) and water (2 mL), then to the suspension, iron powder (470 mg) and ammonium chloride (450 mg) were added, and the mixture was stirred at 80°C for 2 hours. The reaction mixture was cooled to room temperature, filtered through Celite, the mother liquor was dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. This crude product was dissolved in dichloromethane (14 mL), then to the solution, di-tert-butyl dicarbonate (612 mg) and N,N-diisopropylethylamine (0.39 mL) were added, and the mixture was stirred at room temperature for 1 hour. Water was added to the reaction solution, the mixture was extracted with ethyl acetate, the organic layer was dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (667 mg).
MS: m/z 294.1 $(M\text{-}tBu+H)^+$.

Step 3: tert-Butyl N-[3,3-difluoro-2-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]propyl]carbamate

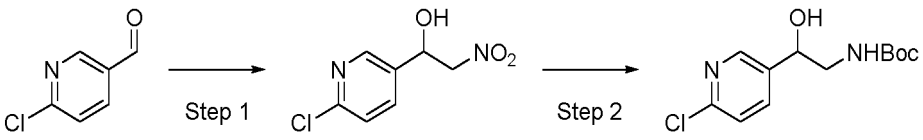
[0245] tert-Butyl N-[2-(4-bromophenyl)-3,3-difluoropropyl]carbamate (667 mg) was dissolved in 1,4-dioxane (19 mL), then to the solution, bis (pinacolato)diboron (629 mg), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium (139 mg) and potassium acetate (561 mg) were added, and the mixture was stirred at 100°C for 3 hours. The reaction mixture was cooled to room temperature, filtered through Celite, and concentrated under reduced pressure to obtain a crude product of the title compound.

[Reference Example 3]

tert-Butyl N-[2-(6-chloropyridin-3-yl)-2-hydroxyethyl]carbamate

[0246]

[Chem. 39]



Step 1: 1-(6-Chloropyridin-3-yl)-2-nitroethanol

[0247] Nitromethane (3 mL) and triethylamine (3 mL) were added to 6-chloropyridin-3-carbaldehyde (1 g), and the mixture was stirred at room temperature for 1 hour. The reaction mixture was concentrated under reduced pressure, and the crude product was used in the next reaction without further purification.

Step 2: tert-Butyl N-[2-(6-chloropyridin-3-yl)-2-hydroxyethyl]carbamate

[0248] The crude product obtained in Step 1 was dissolved in THF (10 mL), then to the solution, zinc powder (2.31 g)

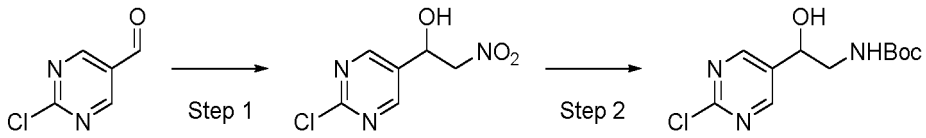
and acetic acid (3 mL) were added, and the mixture was stirred at room temperature for 1 hour. The reaction mixture was filtered through Celite and then concentrated under reduced pressure. This crude product was dissolved in dichloromethane (14 mL), then to the solution, di-tert-butyl dicarbonate (1.54 g) and N,N-diisopropylethylamine (2 mL) were added, and the mixture was stirred at room temperature for 16 hours. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by silica gel column chromatography to obtain the title compound (651 mg).
MS: m/z 273.2 $(M+H)^+$.

[Reference Example 4]

tert-Butyl N-[2-(2-chloropyrimidin-5-yl)-2-hydroxyethyl]carbamate

[0249]

[Chem. 40]



Step 1: 1-(2-Chloropyrimidin-5-yl)-2-nitroethanol

[0250] Nitromethane (1 mL) and triethylamine (2 mL) were added to 2-chloropyrimidine-5-carbaldehyde (428 mg), and the mixture was stirred at room temperature for 2 hours. The reaction mixture was concentrated under reduced pressure, and the crude product was used in the next reaction without further purification.

Step 2: tert-Butyl N-[2-(2-chloropyrimidin-5-yl)-2-hydroxyethyl]carbamate

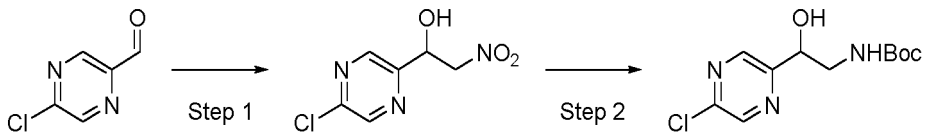
[0251] The crude product obtained in Step 1 was dissolved in THF (5 mL), then to the solution, zinc powder (981 mg) and acetic acid (0.86 mL) were added, and the mixture was stirred at room temperature for 2 hours. The reaction mixture was filtered through Celite and then concentrated under reduced pressure. This crude product was dissolved in dichloromethane (5 mL), then to the solution, di-tert-butyl dicarbonate (1.31 g) and N,N-diisopropylethylamine (1.6 mL) were added, and the mixture was stirred at room temperature for 2 hours. Water was added to the reaction mixture, the mixture was extracted with ethyl acetate. The organic layer was dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the title compound (208 mg). MS: m/z 274.1 $(M+H)^+$.
^{1}H-NMR ($CDCl_3$) δ: 8.64 (2H, s), 4.96-4.94 (2H, m), 3.55-3.51 (1H, m), 3.34-3.27 (1H, m), 1.45 (9H, s).

[Reference Example 5]

tert-Butyl N-[2-(5-chloropyrazin-2-yl)-2-hydroxyethyl]carbamate

[0252]

[Chem. 41]



Step 1: 1-(5-Chloropyrazin-2-yl)-2-nitroethanol

[0253] Nitromethane (1 mL) and triethylamine (1 mL) were added to 5-chloropyrazine-2-carbaldehyde (826 mg), and the mixture was stirred at room temperature for 1 hour. The reaction mixture was concentrated under reduced pressure,

and the crude product was used in the next reaction without further purification.

Step 2: tert-Butyl N-[2-(5-chloropyrazin-2-yl)-2-hydroxyethyl]carbamate

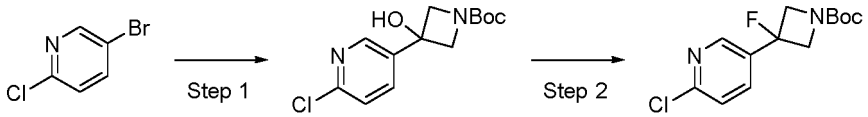
[0254] The crude product obtained in Step 1 was dissolved in THF (5 mL), the solution was cooled to 0°C, then to the solution, di-tert-butyl dicarbonate (1.06 g), zinc powder (792 mg) and acetic acid (0.7 mL) were added, and then the mixture was stirred at room temperature for 16 hours. The reaction mixture was filtered through Celite, water was added to the filtrate, and the mixture was extracted with ethyl acetate. The organic layer was dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the title compound (57.5 mg).
MS: m/z 218.1 $(M-tBu+H)^+$.

[Reference Example 6]

tert-Butyl 3-(6-chloropyridin-3-yl)-3-fluoroazetidine-1-carboxylate

[0255]

[Chem. 42]



Step 1: tert-Butyl 3-(6-chloropyridin-3-yl)-3-hydroxyazetidine-1-carboxylate

[0256] 5-Bromo-2-chloropyridine (385 mg) was dissolved in THF (10 mL), the solution was cooled to -78°C, and to the solution, n-butyllithium (1.2 mL) was added dropwise. After stirring at the same temperature for 1 hour, then to the solution, a solution (2 mL) of 1-(tert-butoxycarbonyl)-3-azetidineone (342 mg) in THF was added, and the temperature of the solution was raised to room temperature over 4 hours. A saturated aqueous solution of ammonium chloride was added to the reaction mixture, the mixture was extracted with ethyl acetate, the organic layer was dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (209 mg).
MS: m/z 285.0 $(M+H)^+$.

Step 2: tert-Butyl 3-(6-chloropyridin-3-yl)-3-fluoroazetidine-1-carboxylate

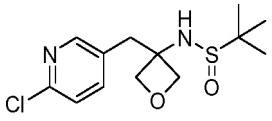
[0257] tert-Butyl 3-(6-chloropyridin-3-yl)-3-hydroxyazetidine-1-carboxylate (100 mg) was dissolved in dichloromethane (1.8 mL), the solution was cool to -78°C, then to the solution bis(2-methoxyethyl)aminosulfur trifluoride (0.078 mL) was added, and the mixture was stirred at the same temperature for 2 hours. The reaction mixture was heated to room temperature, then to the solution, saturated aqueous sodium hydrogen carbonate was added, and the mixture was extracted with ethyl acetate. The organic layer was dried over anhydrous magnesium sulfate and the solution was concentrated under reduced pressure to obtain a crude product of the title compound (40 mg).
MS: m/z 287.0 $(M+H)^+$.

[Reference Example 7]

N-[3-[(6-Chloropyridin-3-yl)methyl]oxetan-3-yl]-2-methylpropane-2-sulfinamide

[0258]

[Chem. 43]



[0259] 2-Chloro-5-iodopyridine (479 mg) was dissolved in THF (10 mL) and to the solution, isopropylmagnesium bromide (1 M solution in THF, 2.0 mL) was added dropwise at 0°C. After stirring the solution at the same temperature for 1 hour, then to the solution, copper(I) iodide (38.1 mg) was added, and the mixture was cooled to -30°C. A solution (2 mL) of 1-tert-butylsulfinyl-5-oxa-1-azaspiro[2.3]hexane (189 mg) in THF was added dropwise to the reaction mixture, the mixture was heated to room temperature, and the mixture was stirred for 2 hours. A saturated aqueous solution of ammonium chloride was added to the reaction mixture, the mixture was extracted with ethyl acetate, the organic layer was dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the title compound (108 mg).

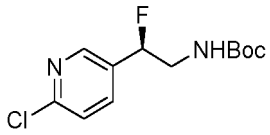
MS: m/z 303.1 $(M+H)^+$.
^{1}H-NMR ($CDCl_3$) δ: 8.33 (1H, s), 7.71 (1H, d, J = 7.3 Hz), 7.30 (1H, d, J = 8.2 Hz), 4.83 (1H, d, J = 6.4 Hz), 4.66-4.56 (3H, m), 3.59 (1H, s), 3.41 (2H, q, J = 14.5 Hz), 1.22 (9H, s).

[Reference Example 8]

tert-Butyl N-[(2R)-2-(6-chloropyridin-3-yl)-2-fluoroethyl]carbamate

[0260]

[Chem. 44]



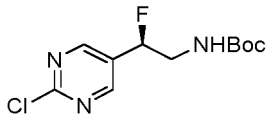
[0261] tert-Butyl N-[(2S)-2-(6-chloropyridin-3-yl)-2-hydroxyethyl]carbamate (164 mg) obtained by chiral separation of the racemic compound of Reference Example 3 was added to dichloromethane (3 mL), and to the mixture, bis(2-methoxyethyl)aminosulfur trifluoride (0.13 mL) was added dropwise at 0°C. After stirring the mixture at the same temperature for 1 hour, the reaction mixture was directly purified by silica gel column chromatography to obtain the title compound (37.5 mg).
MS: m/z 275.1 $(M+H)^+$.

[Reference Example 9]

tert-Butyl N-[(2R)-2-(2-chloropyrimidin-5-yl)-2-fluoroethyl]carbamate

[0262]

[Chem. 45]



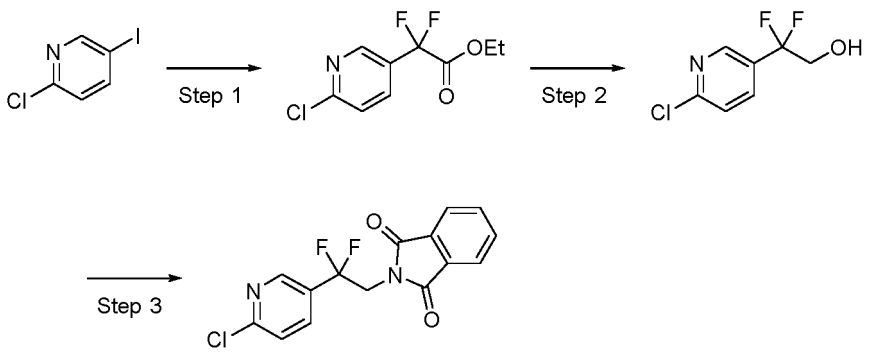
[0263] tert-Butyl N-[(2S)-2-(2-chloropyrimidin-5-yl)-2-hydroxyethyl]carbamate (547 mg) obtained by chiral separation of the racemic compound of Example 4 was dissolved in dichloromethane (10 mL), and to the solution, bis(2-methoxyethyl)aminosulfur trifluoride (0.44 mL) was added dropwise at 0°C. After stirring the mixture at the same temperature for 1 hour, the reaction mixture was directly purified by silica gel column chromatography to obtain the title compound (83.3 mg).
MS: m/z 276.2 $(M+H)^+$.

[Reference Example 10]

2-[2-(6-Chloropyridin-3-yl)-2,2-difluoroethyl]isoindole-1,3-dione

[0264]

[Chem. 46]



Step 1: Ethyl 2-(6-chloropyridin-3-yl)-2,2-difluoroacetate

[0265] 2-Chloro-5-iodopyridine (2 g) was dissolved in DMSO (33 mL), then to the solution, ethyl bromodifluoroacetate (1.87 g) and copper powder (1.33 g) were added, and the mixture was stirred at 80°C for 16 hours. The reaction mixture was cooled to room temperature, an aqueous disodium hydrogen phosphate solution was added to the solution, the mixture was extracted with ethyl acetate, the organic layer was dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (958 mg).
MS: m/z 236.1 $(M+H)^+$.

Step 2: 2-(6-Chloropyridin-3-yl)-2,2-difluoroethanol

[0266] Ethyl 2-(6-chloropyridin-3-yl)-2,2-difluoroacetate (958 mg) was dissolved in methanol (20 mL), the solution was cooled to 0°C, and to the solution, sodium borohydride (308 mg) was added. The mixture was stirred at room temperature for 1 hour. Water was added to the reaction mixture, the mixture was extracted with ethyl acetate, the organic layer was dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (493 mg).
MS: m/z 194.1 $(M+H)^+$.

Step 3: 2-[2-(6-Chloropyridin-3-yl)-2,2-difluoroethyl]isoindole-1,3-dione

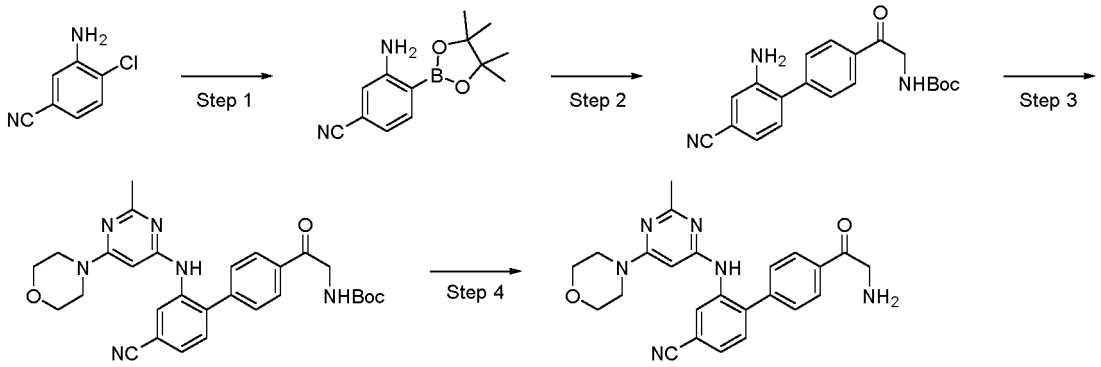
[0267] 2-(6-Chloropyridin-3-yl)-2,2-difluoroethanol (493 mg), phthalimide (487 mg) and triphenylphosphine (1 g) were suspended in THF (5 mL), then to the suspension, diisopropyl azodicarboxylate (0.74 mL) was added dropwise, and the mixture was stirred at room temperature for 16 hours. Water was added to the reaction mixture, the mixture was extracted with ethyl acetate, the organic layer was dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the title compound (395 mg). MS: m/z 323.1 $(M+H)^+$.

[Example 1]

4-[4-(2-Aminoacetyl)phenyl]-3-[(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)amino]benzonitrile (Compound No. 4)

[0268]

[Chem. 47]



Step 1: 3-Amino-4-(4,4,5,5-tetramethyl-1,3,2-dioxaboran-2-yl)benzonitrile

[0269] 3-Amino-4-chlorobenzonitrile (700 mg, 4.59 mmol) was dissolved in 1,4-dioxane (23 mL), then to the solution, bis(pinacolato)diboron (1.28 g, 5.05 mmol), tris(dibenzylideneacetone)dipalladium (126 mg, 0.14 mmol), tricyclohexylphosphonium tetrafluoroborate (101 mg, 0.28 mmol) and potassium acetate (1.35 g, 13.8 mmol) were added, and the mixture was stirred at 100°C for 15 hours. The reaction mixture was cooled to room temperature and filtered through Celite, then the mother liquor was extracted with ethyl acetate, the organic layer was dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (541 mg, 48%).
^{1}H-NMR ($CDCl_3$) δ: 7.65 (1H, d, J = 7.3 Hz), 6.89 (1H, d, J = 7.8 Hz), 6.81 (1H, s), 4.93 (2H, brs), 1.35 (12H, s).

Step 2: tert-Butyl (2-(2'-amino-4'-cyano-[1,1'-biphenyl]-4-yl)-2-oxoethyl)carbamate

[0270] To a solution of 3-amino-4-(4,4,5,5-tetramethyl-1,3,2-dioxaboran-2-yl)benzonitrile (245 mg, 1.00 mmol) in toluene/water (= 4/1, 5 mL), tert-butyl N-[2-(4-bromophenyl)-2-oxo-ethyl]carbamate (315 mg, 1.00 mmol), tetrakis(triphenylphosphine)palladium (57.9 mg, 0.050 mmol) and potassium carbonate (416 mg, 3.00 mmol) were added, and the mixture was stirred at 80°C for 2 hours. The reaction mixture was cooled to room temperature and filtered through Celite. Water was added to the mother liquor, the mixture was extracted with ethyl acetate, the organic layer was dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (280 mg, 80%).
MS: m/z 296.1 $(M\text{-}tBu+H)^+$.

Step 3: tert-Butyl (2-(4'-cyano-2'-((2-methyl-6-morpholinopyrimidin-4-yl) amino)-[1,1'-biphenyl]-4-yl)-2-oxoethyl)carbamate

[0271] tert-Butyl (2-(2'-amino-4'-cyano-[1,1'-biphenyl]-4-yl)-2-oxoethyl)carbamate (50.8 mg, 0.145 mmol) was dissolved in toluene (2 mL), then to the solution, 4-(6-chloro-2-methylpyrimidin-4-yl)morpholine (30.9 mg, 0.145 mmol), tris(dibenzylideneacetone)dipalladium (6.6 mg, 0.072 mmol), 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (8.4 mg, 0.015 mmol) and sodium tert-butoxide (27.8 mg, 0.289 mmol) were added, and the mixture was stirred at 150°C under microwave irradiation for 1.5 hours. The reaction mixture was cooled to room temperature and filtered through Celite, and then the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.

Step 4: 4-[4-(2-Aminoacetyl)phenyl]-3-[(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)amino]benzonitrile

[0272] Dichloromethane (2 mL) and TFA (0.5 mL) were added to the crude product obtained in Step 3, and the mixture was stirred at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (2.09 mg).

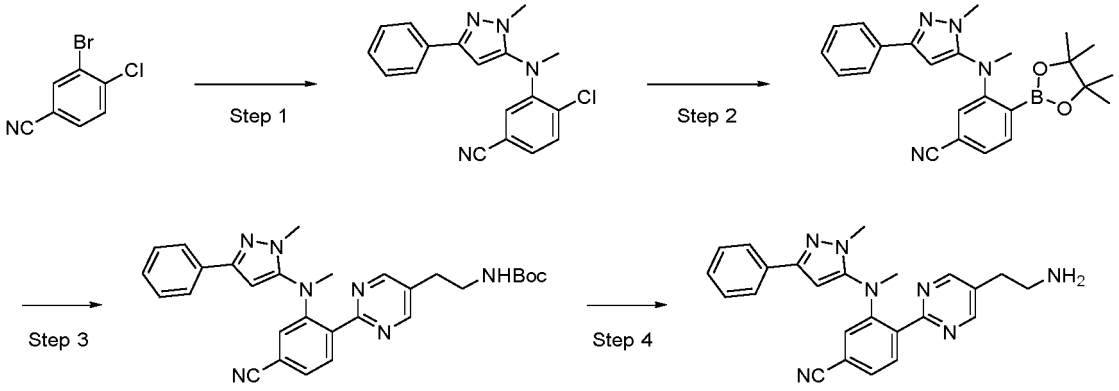
Exact MS: 428.2
Obs. MS $(M+H)^+$: 429.4

[Example 2]

4-[5-(2-Aminoethyl)pyrimidin-2-yl]-3-[methyl-(2-methyl-5-phenylpyrazol-3-yl)amino]benzonitrile (Compound No. 6)

[0273]

[Chem. 48]



Step 1: 4-Chloro-3-[methyl-(2-methyl-5-phenylpyrazol-3-yl)amino]benzonitrile

[0274] 1,4-Dioxane (6.7 mL) was added to 3-bromo-4-chlorobenzonitrile (578 mg, 2.67 mmol) and N,2-dimethyl-5-phenylpyrazole-3-amine (500 mg, 2.67 mmol), and to the mixture, tris(dibenzylideneacetone)dipalladium (122 mg, 0.134 mmol), 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (232 mg, 0.401 mmol), and cesium carbonate (2.18 g, 6.68 mmol) were added, and the mixture was stirred at 100°C for 16 hours. The reaction mixture was cooled to room temperature, and filtered through Celite, and then the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (512 mg, 59%).
MS: m/z 323.1 $(M+H)^+$.

Step 2: 3-[Methyl-(2-methyl-5-phenylpyrazol-3-yl)amino]-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile

[0275] 4-Chloro-3-[methyl-(2-methyl-5-phenylpyrazol-3-yl)amino]benzonitrile (256 mg, 0.792 mmol) was dissolved in 1,4-dioxane (2.6 mL), then to the solution, bis(pinacolato)diboron (302 mg, 1.19 mmol), bis(tricyclohexylphosphine)palladium dichloride (58.5 mg, 0.0792 mmol), and potassium acetate (233 mg, 2.38 mmol) were added, and the mixture was stirred at 100°C for 2 hours. The reaction mixture was cooled to room temperature, and filtered through Celite, and then the solution was concentrated under reduced pressure. The obtained crude product was used in the next reaction without further purification.
MS: m/z 415.0 $(M+H)^+$.

Step 3: tert-Butyl N-[2-[2-[4-cyano-2-[methyl-(2-methyl-5-phenylpyrazol-3-yl)amino]phenyl]pyrimidin-5-yl]ethyl]carbamate

[0276] The crude product obtained in Step 2 was dissolved in 1,4-dioxane (2.6 mL), then to the solution, tert-butyl N-[2-(2-chloropyrimidin-5-yl)ethyl]carbamate (50.0 mg, 0.194 mmol), tetrakis(triphenylphosphine)palladium (22.4 mg, 0.0194 mmol), potassium carbonate (80.4 mg, 0.582 mmol) and water (0.1 mL) were added, and the mixture was stirred at 100°C for 1 hour. The reaction mixture was cooled to room temperature, ethyl acetate and water were added to the mixture, and the mixture was extracted. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.
MS: m/z 510.0 $(M+H)^+$.

Step 4: 4-[5-(2-Aminoethyl)pyrimidin-2-yl]-3-[methyl-(2-methyl-5-phenylpyrazol-3-yl)amino]benzonitrile

[0277] Dichloromethane (1 mL) and TFA (0.5 mL) were added to the crude product obtained in Step 3, and the mixture was stirred at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure, and

the crude product was purified by HPLC to obtain the target compound (48.3 mg).

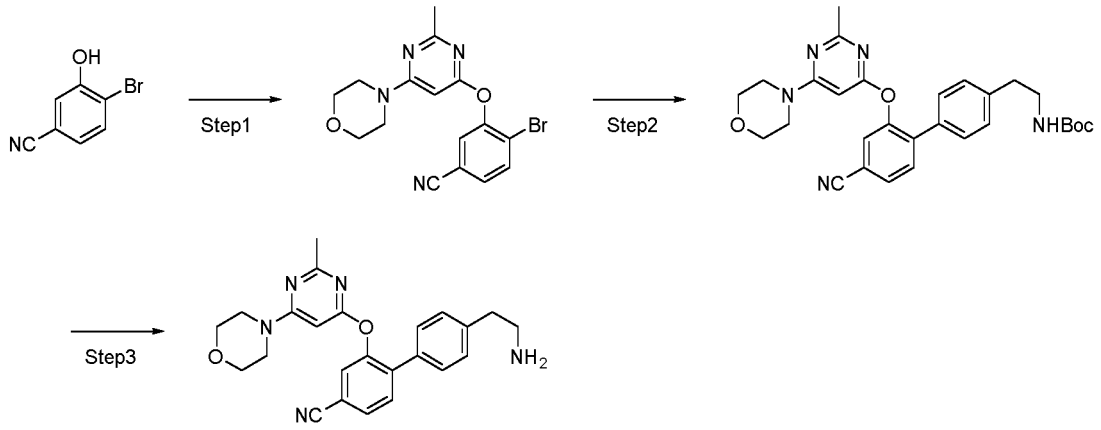
Exact MS: 409.2
Obs. MS $(M+H)^+$: 410.4

[Example 3]

4-[4-(2-Aminoethyl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile (Compound No. 7)

[0278]

[Chem. 49]



Step 1: 4-Bromo-3-((2-methyl-6-morpholinopyrimidin-4-yl)oxy)benzonitrile

[0279] 4-Bromo-3-hydroxybenzonitrile (1.19 g, 6.0 mmol) was dissolved in DMF (10 mL), then to the solution, 4-(6-chloro-2-methylpyrimidin-4-yl)morpholine (1.28 g, 6.0 mmol) and potassium carbonate (2.49 g, 18 mmol) were added to the mixture, and the mixture was stirred at 150°C for 23 hours. The reaction mixture was cooled to room temperature, water was added, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified on a silica gel column to obtain the target compound (1.23 g, 54%).

Step 2: tert-Butyl (2-(4'-cyano-2'-((2-methyl-6-morpholinopyrimidin-4-yl)oxy)-[1,1'-biphenyl]-4-yl)ethyl)carbamate

[0280] 4-Bromo-3-((2-methyl-6-morpholinopyrimidin-4-yl)oxy)benzonitrile (110 mg, 0.29 mmol) was dissolved in toluene/water (= 4/1) mixed solution (2.5 mL), then to the solution, tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaboran-2-yl)phenethylcarbamate (132 mg, 0.38 mmol), tetrakistriphenylphosphine palladium (16.9 mg, 0.015 mmol) and potassium carbonate (121 mg, 0.88 mmol) were added, and the mixture was stirred at 110°C for 10 hours. The reaction mixture was cooled to room temperature, water was added to the solution, and the mixture was extracted with ethyl acetate. The organic layer was dried over anhydrous magnesium sulfate and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (140 mg, 93%).
MS: m/z 516.3 $(M+H)^+$.

Step 3: 4-[4-(2-Aminoethyl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile

[0281] tert-Butyl (2-(4'-cyano-2'-((2-methyl-6-morpholinopyrimidin-4-yl)oxy)-[1,1'-biphenyl]-4-yl)ethyl)carbamate (140 mg, 0.27 mmol) was dissolved in 1,4-dioxane (2 mL), then to the solution, a 4 M (= mol/L) hydrochloric acid/1,4-dioxane solution (2 mL) was added dropwise, and the mixture was stirred at room temperature for 1 hour. The reaction mixture was concentrated under reduced pressure, the crude product was dissolved in a mixed solution of ethyl acetate (50 mL) and 2 M hydrochloric acid (20 mL), and the target compound was back-extracted into an aqueous layer. Then, methanol/dichloromethane (= 1/4) mixed solution (50 mL) and a 2 M aqueous sodium hydroxide solution (22 mL) were added to the mixture and the target compound was extracted into an organic phase. The organic layer was dried over anhydrous

sodium sulfate and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (84.1 mg).

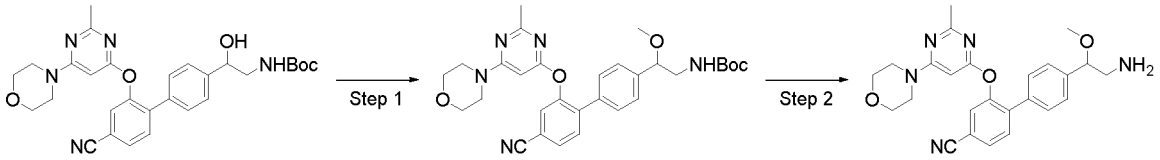
Exact MS: 415.2
Obs. MS $(M+H)^+$: 416.2

[Example 4]

4-[4-(2-Amino-1-methoxyethyl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile (Compound No. 11)

[0282]

[Chem. 50]



Step 1: tert-Butyl (2-(4'-cyano-2'-((2-methyl-6-morpholinopylimidin-4-yl)oxy)-[1,1'-biphenyl]-4-yl)-2-methoxyethyl)carbamate

[0283] tert-Butyl (2-(4'-cyano-2'-((2-methyl-6-morpholinopyrimidin-4-yl)oxy)-[1,1'-biphenyl]-4-yl)-2-hydroxyethyl)carbamate (29 mg, 0.055 mmol) synthesized by the same method as in Example 3 was dissolved in DMF (1 mL), then to the solution, sodium hydride (2.7 mg) was added, and the mixture was stirred at room temperature for 5 minutes. Iodomethane (4.2 μL, 0.066 mmol) was added to this reaction mixture, and the mixture was stirred at room temperature for 1 hour. Water was added to the reaction mixture, the mixture was stirred, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.

Step 2: 4-[4-(2-Amino-1-methoxyethyl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile

[0284] The crude product obtained in Step 1 was dissolved in dichloromethane (2 mL), then to the solution, TFA (0.5 mL) was added, and the mixture was stirred at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (8.7 mg).

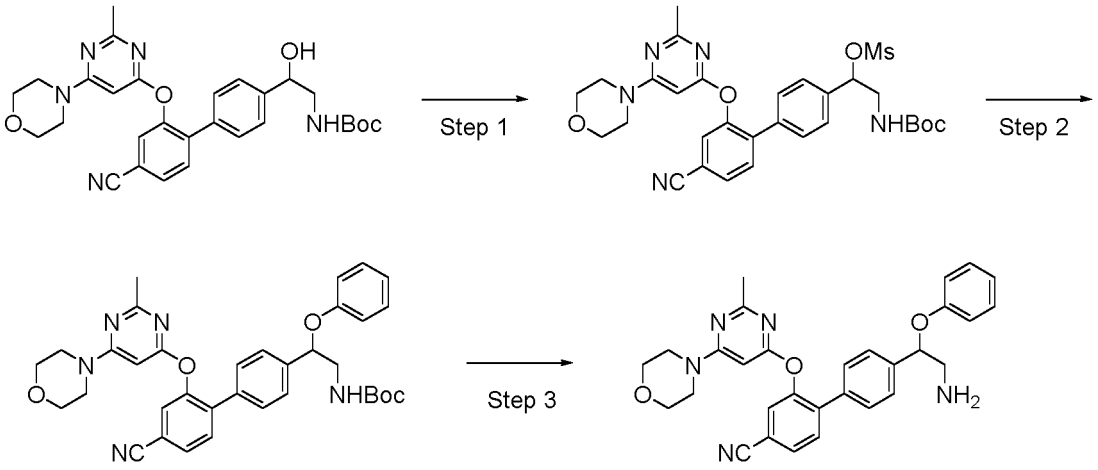
Exact MS: 445.2
Obs. MS $(M+H)^+$: 446.2

[Example 5]

4-[4-(2-Amino-1-phenoxyethyl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile (Compound No. 13)

[0285]

[Chem. 51]



Step 1: 2-((tert-Butoxycarbonyl)amino)-1-(4'-cyano-2'-((2-methyl-6-morpholinopyrimidin-4-yl)oxy)-[1,1'-biphenyl]-4-yl)ethylmethanesulfonate

[0286] tert-Butyl (2-(4'-cyano-2'-((2-methyl-6-morpholinopyrimidin-4-yl)oxy)-[1,1'-biphenyl]-4-yl)-2-hydroxyethyl)carbamate (60.9 g, 0.115 mmol) synthesized by the same method as in Example 3 was dissolved in THF (2 mL), then to the solution, triethylamine (48 μL, 0.34 mmol) and methanesulfonyl chloride (11 μL, 0.14 mmol) were added, and the mixture was stirred at room temperature for 1 hour. The reaction mixture was diluted with water and ethyl acetate, and extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The crude product was used in the next reaction without further purification.
MS: m/z 610.3 $(M+H)^+$.

Step 2: tert-Butyl (2-(4'-cyano-2'-((2-methyl-6-morpholinopyrimidin-4-yl)oxy)-[1,1'-biphenyl]-4-yl)-2-phenoxyethyl)carbamate

[0287] The crude product obtained in Step 1 was dissolved in DMF (2 mL), then to the solution, phenol (10.8 mg, 0.115 mmol) and potassium carbonate (47.5 mg, 0.34 mmol) were added, and the mixture was stirred at 100°C for 16 hours. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The crude product was used in the next reaction without further purification.
MS: m/z 608.3 $(M+H)^+$.

Step 3: 4-[4-(2-Amino-1-phenoxyethyl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile

[0288] The crude product obtained in Step 2 was dissolved in dichloromethane (2 mL), then to the solution, TFA (0.5 mL) was added, and the mixture was stirred at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (5.5 mg).

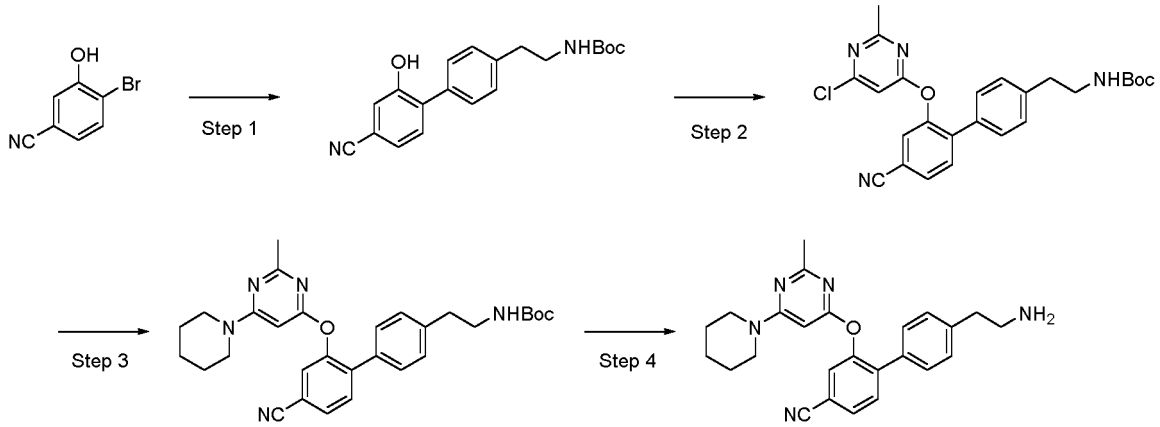
Exact MS: 507.2
Obs. MS $(M+H)^+$: 508.2

[Example 6]

4-[4-(2-Aminoethyl)phenyl]-3-(2-methyl-6-piperidin-1-ylpyrimidin-4-yl)oxybenzonitrile (Compound No. 17)

[0289]

[Chem. 52]



Step 1: tert-Butyl (2-(4'-cyano-2'-hydroxy-[1,1'-biphenyl]-4-yl)ethyl)carbamate

[0290] To a solution (50 mL) of 4-bromo-3-hydroxybenzonitrile (8.6 g, 43.4 mmol) in toluene/water (=9/1), tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaboran-2-yl)phenethylcarbamate (22.7 g, 65.1 mmol), tetrakistriphenylphosphine palladium (5.0 g, 4.34 mmol), and potassium carbonate (11.9 g, 86.1 mmol) were added, and the mixture was stirred at 90°C for 16 hours. The reaction mixture was cooled to room temperature, filtered through Celite, the mother liquor was extracted with ethyl acetate, the organic layer was dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (5.0 g, 35%).

Step 2: tert-Butyl (2-(2'-((6-chloro-2-methylpyrimidin-4-yl)oxy)-4'-cyano-[1,1'-biphenyl]-4-yl)ethyl)carbamate

[0291] To a solution of tert-butyl (2-(4'-cyano-2'-hydroxy-[1,1'-biphenyl]-4-yl)ethyl)carbamate (2.8 g, 8.3 mmol) in DMF (15 mL), 4,6-dichloro-2-methylpyrimidine (1.35 g, 8.28 mmol) and cesium carbonate (5.38 g, 16.6 mmol) were added, and the mixture was stirred overnight at room temperature. Water and ethyl acetate were added to the reaction mixture, the mixture was extracted with ethyl acetate, the organic layer was dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (1.8 g, 46%).
MS: m/z 464.8 $(M+H)^+$.

Step 3: tert-Butyl (2-(4'-cyano-2'-((2-methyl-6-(piperidin-1-yl)pyrimidin-4-yl)oxy)-[1,1'-biphenyl]-4-yl)ethyl)carbamate

[0292] tert-Butyl (2-(2'-((6-chloro-2-methylpyrimidin-4-yl)oxy)-4'-cyano-[1,1'-biphenyl]-4-yl)ethyl)carbamate (100 mg, 0.216 mmol) was dissolved in DMF (3 mL), then to the solution, piperidine (0.043 mL, 0.432 mmol) and cesium carbonate (140 mg, 0.431 mmol) were added, and the mixture was stirred at room temperature for 16 hours. Water was added to the reaction mixture, the mixture was extracted with dichloromethane, the organic layer was dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.
MS: m/z 514.3 $(M+H)^+$.

Step 4: 4-[4-(2-Aminoethyl)phenyl]-3-(2-methyl-6-piperidin-1-ylpyrimidin-4-yl)oxybenzonitrile

[0293] TFA (0.5 mL) was added to a solution of the crude product obtained in Step 3 in dichloromethane (2 mL), and the mixture was stirred at room temperature for 2 hours. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (57.2 mg).

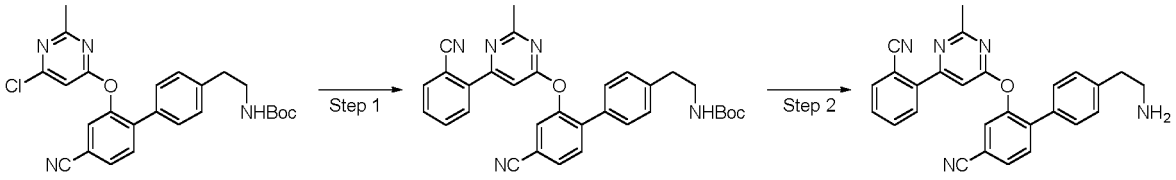
Exact MS: 413.2
Obs. MS $(M+H)^+$: 414.0
^{1}H-NMR (DMSO-d_6) δ: 7.73 (1H, d, J = 8.4 Hz), 7.68 (1H, s), 7.61 (1H, d, J = 8.0 Hz), 7.35 (2H, d, J = 7.6 Hz), 7.21 (2H, d, J = 7.6 Hz), 6.03 (1H, s), 3.52 (4H, bs), 2.75-2.78 (2H, m), 2.64 (2H, s), 2.15 (3H, s), 1.59 (2H, s), 1.45 (4H, bs).

[Example 7]

4-[4-(2-Aminoethyl)phenyl]-3-[6-(2-cyanophenyl)-2-methylpyrimidin-4-yl]oxybenzonitrile (Compound No. 21)

[0294]

[Chem. 53]



Step 1: tert-Butyl (2-(4'-cyano-2'-((6-(2-cyanophenyl)-2-methylpyrimidin-4-yl)oxy)-[1,1'-biphenyl]-4-yl)ethyl)carbamate

[0295] An intermediate of tert-butyl (2-(2'-((6-chloro-2-methylpyrimidin-4-yl)oxy)-4'-cyano-[1,1'-biphenyl]-4-yl)ethyl)carbamate (100 mg, 0.215 mmol) obtained in Example 6 was dissolved in 1,4-dioxane (2 mL), then to the solution, potassium carbonate (59 mg, 0.43 mmol), 2-cyanophenylboronic acid (47 mg, 0.32 mmol), and tetrakistriphenylphosphine palladium (20 mg, 0.017 mmol) were added, and the mixture was stirred overnight at 100°C under a nitrogen atmosphere. The reaction mixture was cooled to room temperature and filtered through Celite, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulfate and the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.

Step 2: 4-[4-(2-Aminoethyl)phenyl]-3-[6-(2-cyanophenyl)-2-methylpyrimidin-4-yl]oxybenzonitrile

[0296] The crude product obtained in Step 1 was dissolved in dichloromethane (2 mL), then to the solution, TFA (0.5 mL) was added, and the mixture was stirred at room temperature for 2 hours. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (15.4 mg).

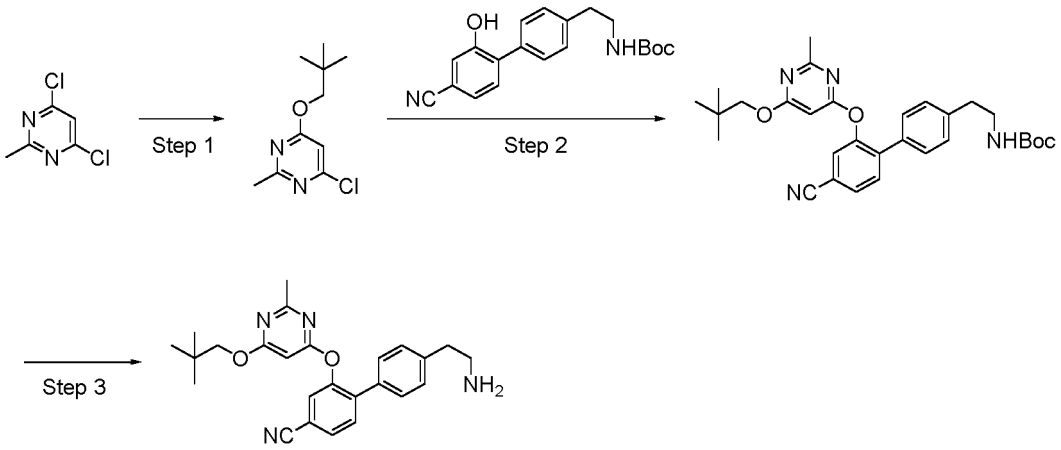
Exact MS: 431.2
Obs. MS $(M+H)^+$: 431.9
^{1}H-NMR (DMSO-d_6) δ: 8.01-7.99 (2H, m), 7.95-7.93 (1H, m), 7.89-7.82 (2H, m), 7.74-7.70 (2H, m), 7.44- 7.39 (3H, m), 7.28-7.23 (2H, m), 3.23 (2H, s), 1.90 (3H, s), 1.23 (2H, s).

[Example 8]

4-[4-(2-Aminoethyl)phenyl]-3-[6-(2,2-dimethylpropoxy)-2-methylpyrimidin-4-yl]oxybenzonitrile (Compound No. 47)

[0297]

[Chem. 54]



Step 1: 4-Chloro-2-methyl-6-(neopentyloxy)pyrimidine

[0298] To a stirred mixture of sodium hydride (82 mg, 3.4 mmol) suspended in THF (4 mL), a solution of 2,2-dimethylpropan-1-ol (323 mg, 3.68 mmol) in THF (0.5 mL) was added dropwise at room temperature and the mixture was stirred at the same temperature for 15 minutes. The reaction mixture was cooled to 0°C, a solution of 4,6-dichloro-2-methylpyrimidine (400 mg, 2.45 mmol) in THF (0.5 mL) was added dropwise to the mixture, and the mixture was stirred at 0°C for 4 hours. A saturated aqueous ammonium chloride solution was added to the reaction mixture, and the mixture was extracted with diethyl ether. The organic layer was dried over anhydrous sodium sulfate and the solution was concentrated under reduced pressure. The crude product was purified on a silica gel column to obtain the target compound (245 mg, 47%).

Step 2: tert-Butyl (2-(4'-cyano-2'-((2-methyl-6-(neopentyloxy)pyrimidin-4-yl)oxy)-[1,1'-biphenyl]-4-yl)ethyl)carbamate

[0299] tert-Butyl (2-(4'-cyano-2'-hydroxy-[1,1'-biphenyl]-4-yl)ethyl)carbamate (50 mg, 0.148 mmol) was dissolved in DMF (1 mL), then to the solution, 4-chloro-2-methyl-6-(neopentyloxy)pyrimidine (63.5 mg, 0.296 mmol) and cesium carbonate (96.4 mg, 0.296 mmol) were added, and the mixture was stirred at 70°C overnight. Water was added to the reaction mixture, the mixture was extracted with ethyl acetate, the organic layer was dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.
MS: m/z 517.0 $(M+H)^+$.

Step 3: 4-[4-(2-Aminoethyl)phenyl]-3-[6-(2,2-dimethylpropoxy)-2-methylpyrimidin-4-yl]oxybenzonitrile

[0300] Dichloromethane (2 mL) and TFA (0.5 mL) were added to the crude product obtained in Step 2, and the mixture was stirred at room temperature for 3 hours. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (21.4 mg).

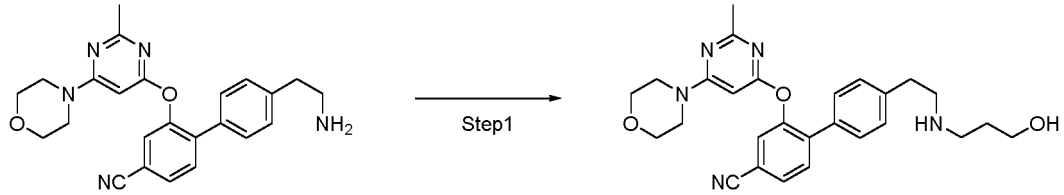
Exact MS: 416.2
Obs. MS $(M+H)^+$: 417.3

[Example 9]

4-[4-[2-(3-Hydroxypropylamino)ethyl]phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile (Compound No. 58)

[0301]

[Chem. 55]



Step 1: 4-[4-[2-(3-Hydroxypropylamino)ethyl]phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile

[0302] 4-[4-(2-Aminoethyl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile (54 mg, 0.13 mmol) obtained in Example 3 was dissolved in DMF (1 mL), then to the solution, 3-bromopropan-1-ol (0.014 ml, 0.16 mmol) and triethylamine (0.055 mL, 0.39 mmol) were added, and the mixture was stirred at 60°C for 3 hours. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by HPLC to obtain the target compound (11.3 mg).

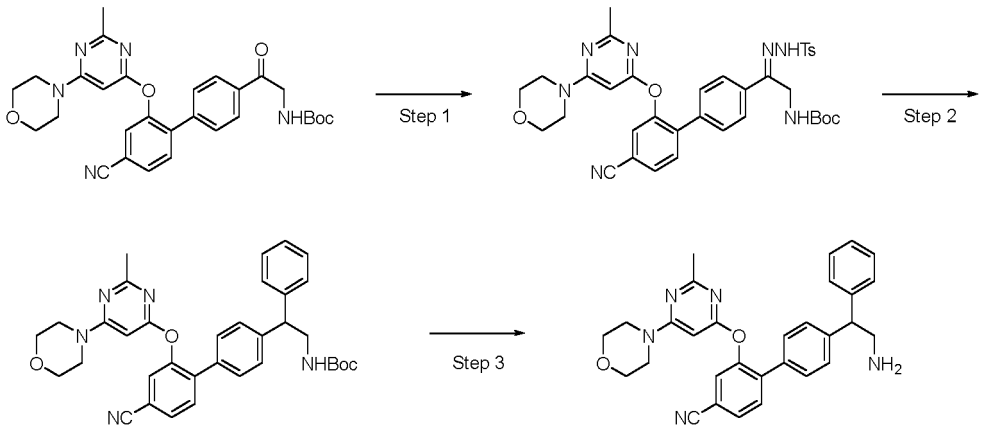
Exact MS: 473.2
Obs. MS $(M+H)^+$: 474.5

[Example 10]

4-[4-(2-Amino-1-phenylethyl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile (Compound No. 59)

[0303]

[Chem. 56]



Step 1: tert-Butyl (2-(4'-cyano-2'-((2-methyl-6-morpholinopyrimidin-4-yl)oxy)-[1,1'-biphenyl]-4-yl)-2-(2-tosylhydrazono)ethyl)carbamate

[0304] tert-Butyl (2-(4'-cyano-2'-((2-methyl-6-morpholinopyrimidin-4-yl)oxy)-[1,1'-biphenyl]-4-yl)-2-oxoethyl)carbamate (855.8 mg, 1.62 mmol) synthesized by the same method in Example 3 was dissolved in toluene (8 mL), then to the solution, p-toluenesulfonyl hydrazide (301 mg, 1.62 mmol) was added, and the mixture was stirred at 110°C for 4 hours. The reaction mixture was concentrated under reduced pressure, and the crude product was used in the next reaction without further purification.
MS: m/z 698.2 $(M+H)^+$.

Step 2: tert-Butyl (2-(4'-cyano-2'-((2-methyl-6-morpholinopyrimidin-4-yl)oxy)-[1,1'-biphenyl]-4-yl)-2-phenylethyl)carbamate

[0305] An aliquot (30 mg) of the crude product obtained in Step 1 was dissolved in 1,4-dioxane (1 mL), then to the solution, phenylboronic acid (11 mg, 0.086 mmol) and potassium carbonate (24 mg, 0.17 mmol) were added, and the mixture was stirred at 110°C for 15 hours. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.
MS: m/z 592.3 $(M+H)^+$.

Step 3: 4-[4-(2-Amino-1-phenylethyl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile

[0306] The crude product obtained in Step 2 was dissolved in dichloromethane (2 mL), then to the solution, TFA (0.5 mL) was added, and the mixture was stirred at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (3.1 mg).

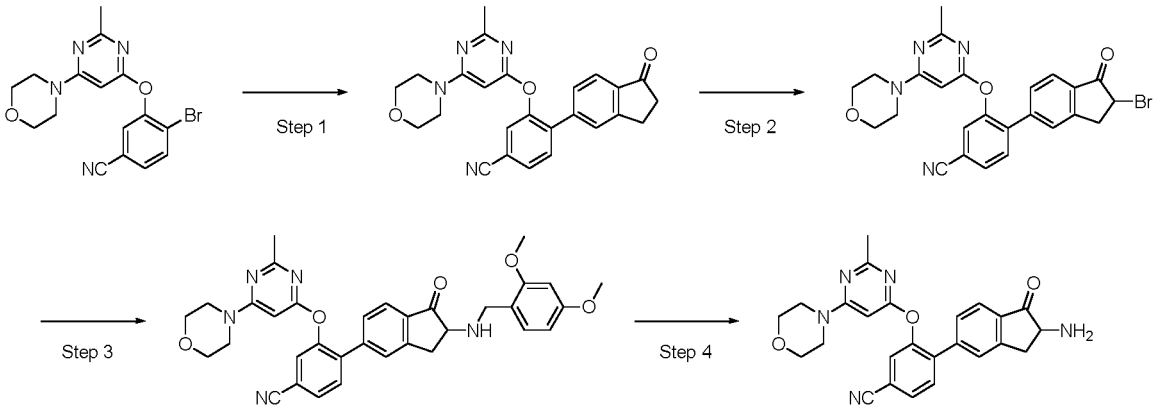
Exact MS: 491.2
Obs. MS $(M+H)^+$: 492.5

[Example 11]

4-(2-Amino-1-oxo-2,3-dihydroinden-5-yl)-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile (Compound No. 131)

[0307]

[Chem. 57]



Step 1: 3-(2-Methyl-6-morpholin-4-ylpyrimidin-4-yl)oxy-4-(1-oxo-2,3-dihydroinden-5-yl)benzonitrile

[0308] 4-Bromo-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile (300 mg, 0.800 mmol) was dissolved in 1,4-dioxane (2 mL), then to the solution, 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,3-dihydroinden-1-one (289 mg, 1.12 mmol), tetrakis(triphenylphosphine)palladium (46.2 mg, 0.0400 mmol), potassium carbonate (332 mg, 2.40 mmol) and water (0.5 mL) were added, and the mixture was stirred at 100°C for 4 hours. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (290 mg, 85%).
MS: m/z 427.2 $(M+H)^+$.

Step 2: 4-(2-Bromo-1-oxo-2,3-dihydroinden-5-yl)-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile

[0309] 3-(2-Methyl-6-morpholin-4-ylpyrimidin-4-yl)oxy-4-(1-oxo-2,3-dihydroinden-5-yl)benzonitrile (290 mg, 0.680 mmol) was dissolved in a mixed solvent (6 mL) of chloroform/ethyl acetate (=1/1), then to the solution, copper(II) bromide (304 mg, 1.36 mmol) was added, and the mixture was stirred at 90°C for 7 hours. The reaction mixture was cooled to room temperature and filtered through Celite, and then the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (26.0 mg, 8%).
MS: m/z 505.1 $(M+H)^+$.

Step 3: 4-[2-[(2,4-Dimethoxyphenyl)methylamino]-1-oxo-2,3-dihydroinden-5-yl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile

[0310] 4-(2-Bromo-1-oxo-2,3-dihydroinden-5-yl)-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile (26.0 mg, 0.0514 mmol) was dissolved in DMF (1 mL), then to the solution, 2,4-dimethoxybenzenemethanamine (12.9 mg, 0.0772 mmol) and triethylamine (0.022 mL, 0.154 mmol) were added, and the mixture was stirred at room temperature for 1 hour. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.

Step 4: 4-(2-Amino-1-oxo-2,3-dihydroinden-5-yl)-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile

[0311] TFA (1 mL) was added to the crude product obtained in Step 3, and the mixture was stirred at 120°C for 10 minutes. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (6.00 mg).

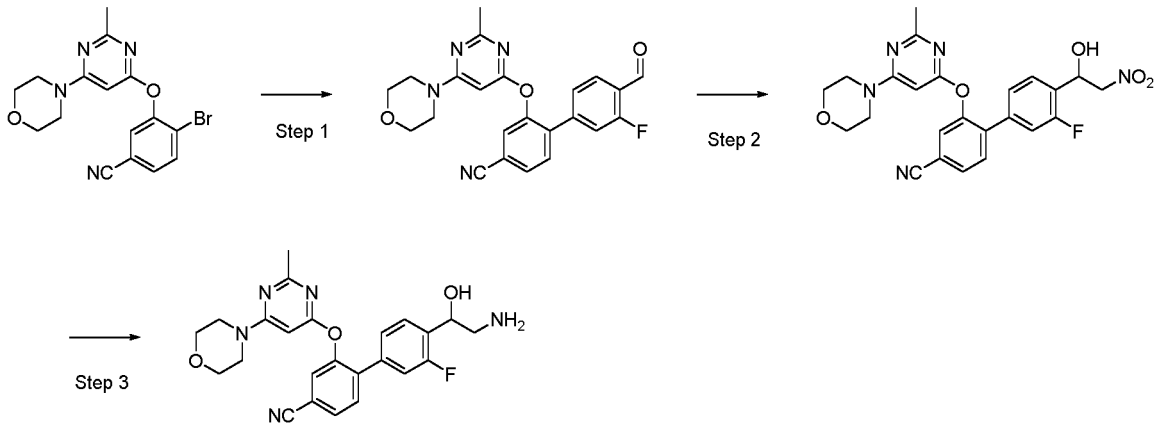
Exact MS: 441.2
Obs. MS $(M+H)^+$: 442.2

[Example 12]

4-[4-(2-Amino-1-hydroxyethyl)-3-fluorophenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile (Compound No. 149)

[0312]

[Chem. 58]



Step 1: 4-(3-fluoro-4-formylphenyl)-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile

[0313] 4-Bromo-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile (188 mg, 0.500 mmol) was dissolved in 1,4-dioxane (4 mL), then to the solution, 2-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde (250 mg, 1.00 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride (36.6 mg, 0.0500 mmol), potassium carbonate (415 mg, 3.00 mmol) and water (1 mL) were added, and the mixture was stirred at 100°C for 30 minutes. The reaction

mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (174 mg, 83%).
MS: m/z 419.2 $(M+H)^+$.

Step 2: 4-[3-Fluoro-4-(1-hydroxy-2-nitroethyl)phenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile

[0314] 4-(3-Fluoro-4-formylphenyl)-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile (174 mg, 0.416 mmol) was dissolved in THF (4 mL), then to the solution, nitromethane (0.5 mL) and triethylamine (1 mL) were added, and the mixture was stirred at room temperature for 2 hours. The reaction solution was concentrated under reduced pressure, and the crude product was used in the next reaction without further purification.
MS: m/z 480.2 $(M+H)^+$.

Step 3: 4-[4-(2-Amino-1-hydroxyethyl)-3-fluorophenyl]-3-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)oxybenzonitrile

[0315] Zinc powder (500 mg, 7.64 mmol) and acetic acid (4 mL) were added to the crude product obtained in Step 2, and the mixture was stirred for 30 minutes. The reaction mixture was filtered through Celite and concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (15.7 mg).

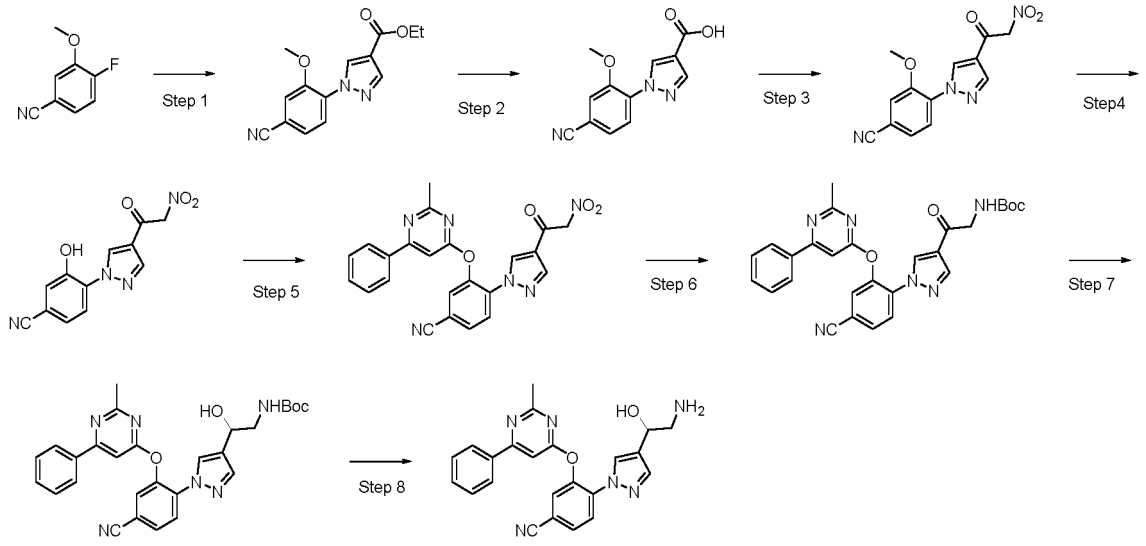
Exact MS: 449.2
Obs. MS $(M+H)^+$: 450.2

[Example 13]

4-[4-[(1R)-2-Amino-1-hydroxyethyl]pyrazol-1-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile (Compound No. 170)

[0316]

[Chem. 59]



Step 1: Ethyl 1-(4-cyano-2-methoxyphenyl)pyrazole-4-carboxylate

[0317] DMSO (120 mL) was added to 4-fluoro-3-methoxybenzonitrile (15.1 g, 100 mmol), ethyl 1H-pyrazole-4-carboxylate (15.4 g, 110 mmol), and potassium carbonate (27.6 g, 200 mmol), and the mixture was stirred at 60°C for 3 hours. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was stirred. The precipitated solid was collected by filtration through a glass filter and dried to obtain the target compound (22.8 g, 84%).

MS: m/z 272.0 $(M+H)^+$.

Step 2: 1-(4-Cyano-2-methoxyphenyl)pyrazole-4-carboxylic acid

[0318] Ethyl 1-(4-cyano-2-methoxyphenyl)pyrazole-4-carboxylate (11.0 g, 40.5 mmol) was dissolved in a mixed solvent of THF (40 mL)/methanol (40 mL), then to the solution, a 2 M aqueous sodium hydroxide solution (40.5 mL, 81.1 mmol) was added, and the mixture was stirred at room temperature for 2 hours. After adding 2M hydrochloric acid to the reaction mixture and stirring the mixture, water was further added to the solution to precipitate the target compound. The target compound was collected by filtration with a glass filter and dried to obtain the target compound (7.38 g, 75%).
MS: m/z 244.0 $(M+H)^+$.

Step 3: 3-Methoxy-4-[4-(2-nitroacetyl)pyrazol-1-yl]benzonitrile

[0319] To 1-(4-cyano-2-methoxyphenyl)pyrazole-4-carboxylic acid (7.38 g, 30.3 mmol), DMF (40 mL) and 1,1'-carbonyldime (5.90 g, 36.4 mmol) were added and the mixture was stirred for 2 hours (reaction mixture A). Nitromethane (2.78 g, 45.5 mmol) and DMF (40 mL) were added to another reaction vessel, sodium hydride (1.59 g, 36.4 mmol) was further added, and the mixture was stirred for 2 hours to separately prepare another solution (reaction mixture B). The reaction mixture B was cooled to 0°C, the reaction mixture A was added dropwise to the reaction mixture B, and then the mixture was heated to 100°C and stirred for 3 hours. The reaction mixture was cooled to room temperature, water was added to the mixture, and the target compound was precipitated. The precipitate was collected by filtration with a glass filter and dried to obtain the target compound (8.70 g, quant.).
MS: m/z 287.0 $(M+H)^+$.

Step 4: 3-Hydroxy-4-[4-(2-nitroacetyl)pyrazol-1-yl]benzonitrile

[0320] 3-Methoxy-4-[4-(2-nitroacetyl)pyrazol-1-yl]benzonitrile (4.50 g, 15.7 mmol) was dissolved in DMF (40 mL), then to the solution, lithium chloride (6.67 g, 157 mmol) was added, and the mixture was stirred at 150°C overnight. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.
MS: m/z 273.0 $(M+H)^+$.

Step 5: 3-(2-Methyl-6-phenylpyrimidin-4-yl)oxy-4-[4-(2-nitroacetyl)pyrazol-1-yl]benzonitrile

[0321] The crude product obtained in Step 4 was dissolved in DMF (40 mL), then to the solution, 4-chloro-2-methyl-6-phenylpyrimidine (3.54 g, 17.3 mmol) and potassium carbonate (4.35 g, 31.4 mmol) were added, and the mixture was stirred at 100°C overnight. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure to obtain the target compound (2.69 g, 39%).
MS: m/z 441.1 $(M+H)^+$.

Step 6: tert-Butyl N-[2-[1-[4-cyano-2-(2-methyl-6-phenylpyrimidin-4-yl)oxyphenyl]pyrazol-4-yl]-2-oxoethyl]carbamate

[0322] THF (40 mL) and acetic acid (1.83 g, 30.5 mmol) were added to 3-(2-methyl-6-phenylpyrimidin-4-yl)oxy-4-[4-(2-nitroacetyl)pyrazol-1-yl]benzonitrile (2.69 g, 6.11 mmol), di-tert-butyl dicarbonate (4.00 g, 18.3 mmol) and zinc powder (2.00 g, 30.5 mmol), and the mixture was stirred at room temperature overnight. The reaction mixture was filtered through Celite, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (540 mg, 17%).
MS: m/z 511.2 $(M+H)^+$.

Step 7: tert-Butyl N-[(2R)-2-[1-[4-cyano-2-(2-methyl-6-phenylpyrimidin-4-yl)oxyphenyl]pyrazol-4-yl]-2-hydroxyethyl]carbamate

[0323] tert-Butyl N-[2-[1-[4-cyano-2-(2-methyl-6-phenylpyrimidin-4-yl)oxyphenyl]pyrazol-4-yl]-2-oxoethyl]carbamate (106 mg, 0.208 mmol) and (S)-5,5-diphenyl-2-methyl-3,4-propano-1,3,2-oxazaborolidine (5.8 mg, 0.021 mmol) were dissolved in dichloromethane (1 mL) and the solution was cooled to 0°C. Dimethyl sulfide borane (47.3 mg, 0.633 mmol)

was added to the reaction mixture, and the mixture was stirred at the same temperature for 10 hours. Methanol and water were added to the reaction mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.
MS: m/z 513.2 $(M+H)^+$.

Step 8: 4-[4-[(1R)-2-Amino-1-hydroxyethyl]pyrazol-1-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile

[0324] The crude product obtained in Step 7 was dissolved in dichloromethane (1 mL), TFA (1 mL) was added to the solution, and the mixture was stirred at room temperature for 1 hour. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (18.6 mg).

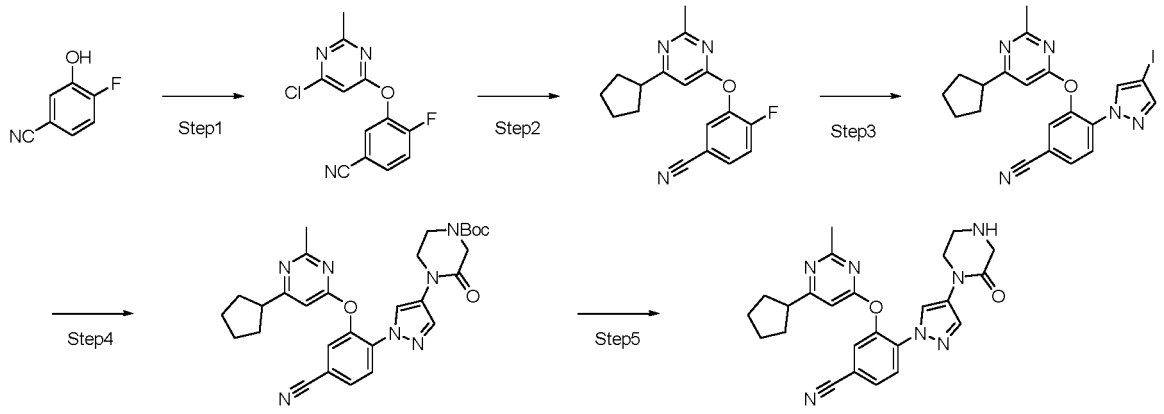
Exact MS: 412.2
Obs. MS $(M+H)^+$: 413.2

[Example 14]

3-(6-Cyclopentyl-2-methylpyrimidin-4-yl)oxy-4-[4-(2-oxopiperazin-1-yl)pyrazol-1-yl]benzonitrile (Compound No. 208)

[0325]

[Chem. 60]



Step 1: 3-(6-Chloro-2-methylpyrimidin-4-yl)oxy-4-fluorobenzonitrile

[0326] 4-Fluoro-3-hydroxybenzonitrile (3.7 g, 27 mmol) was dissolved in DMF (90 mL), then to the solution, 4,6-dichloro-2-methylpyrimidine (6.6 g, 40 mmol) and potassium carbonate (7.5 g, 54 mmol) were added, and the mixture was stirred at 100°C for 2 hours. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified on a silica gel column to obtain the target compound (6.5 g).

MS: m/z 264.1 $(M+H)^+$.
^{1}H-NMR ($CDCl_3$) δ: 7.61 (1H, dq, J = 8.7, 2.1 Hz), 7.56 (1H, dd, J = 7.1, 2.2 Hz), 7.32 (1H, dd, J = 9.5, 8.5 Hz), 6.90 (1H, s), 2.51 (3H, s).

Step 2: 3-(6-Cyclopentyl-2-methylpyrimidin-4-yl)oxy-4-fluorobenzonitrile

[0327] THF (12.6 mL) was added to 3-(6-chloro-2-methylpyrimidin-4-yl)oxy-4-fluorobenzonitrile (1.0 g, 3.79 mmol) and [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride (557 mg, 0.759 mmol), then to the mixture, cyclopentyl zinc bromide (1.22 g, 5.69 mmol) was added dropwise, and the mixture was stirred at 70°C for 1 hour. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous sodium sulfate, and the solution was

concentrated under reduced pressure. The crude product was purified on a silica gel column to obtain the target compound (888 mg).
MS: m/z 298.1 $(M+H)^+$.

Step 3: 3-(6-Cyclopentyl-2-methylpyrimidin-4-yl)oxy-4-(4-iodopyrazol-1-yl)benzonitrile

[0328] 3-(6-Cyclopentyl-2-methylpyrimidin-4-yl)oxy-4-fluorobenzonitrile (100 mg, 0.336 mmol) was dissolved in DMSO (0.5 mL), then to the solution, 4-iodo-1H-pyrazole (65.2 mg, 0.336 mmol) and potassium carbonate (93.0 mg, 0.673 mmol) were added, and the mixture was stirred at 120°C for 2 hours. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified on a silica gel column to obtain the target compound (78.9 mg).
MS: m/z 472.1 $(M+H)^+$.

Step 4: 3-(6-Cyclopentyl-2-methylpyrimidin-4-yl)oxy-4-(4-iodopyrazol-1-yl)benzonitrile

[0329] 3-(6-Cyclopentyl-2-methylpyrimidin-4-yl)oxy-4-(4-iodopyrazol-1-yl)benzonitrile (34.2 mg, 0.0726 mmol) was added to 1,4-dioxane (0.4 mL), then to the solution, tert-butyl 3-oxopiperazine-1-carboxylate (16 mg, 0.080 mmol), copper(I) iodide (2.8 mg, 0.015 mmol), trans-1,2-cyclohexanediamine (1.7 mg, 0.015 mmol) and tripotassium phosphate (46.2 mg, 0.218 mmol) were added, and the mixture was stirred at 110°C for 2 hours. The reaction mixture was cooled to room temperature and filtered through Celite, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.

Step 5: 3-(6-Cyclopentyl-2-methylpyrimidin-4-yl)oxy-4-[4-(2-oxopiperazin-1-yl)pyrazol-1-yl]benzonitrile

[0330] Dichloromethane (1 mL) and TFA (1 mL) were added to the crude product obtained in Step 4, and the mixture was stirred at room temperature for 1 hour. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (7.3 mg).

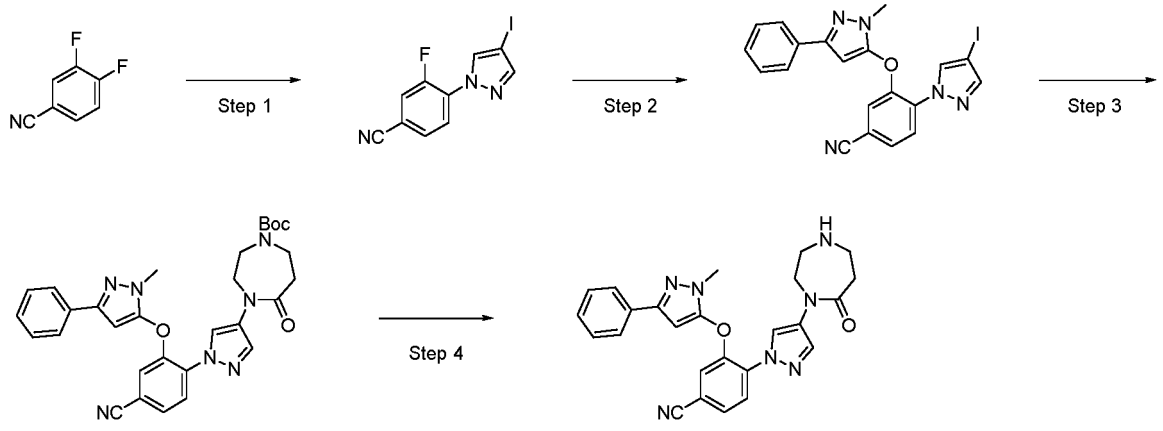
Exact MS: 443.2
Obs. MS $(M+H)^+$: 444.3

[Example 15]

3-(2-Methyl-5-phenylpyrazol-3-yl)oxy-4-[4-(7-oxo-1,4-diazepan-1-yl)pyrazol-1-yl]benzonitrile (Compound No. 219)

[0331]

[Chem. 61]



Step 1: 3-Fluoro-4-(4-iodopyrazol-1-yl)benzonitrile

[0332] DMF (8.6 mL) was added to 3,4-difluorobenzonitrile (430 mg, 3.09 mmol), 4-iodo-1H-pyrazole (500 mg, 2.58 mmol), and cesium carbonate (1.68 g, 5.16 mmol), and the mixture was stirred at 120°C for 3 hours. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (428 mg, 53%).
^{1}H-NMR ($CDCl_3$) δ: 8.18 (1H, d, J = 2.7 Hz), 8.15 (1H, t, J = 8.2 Hz), 7.79 (1H, s), 7.60-7.55 (2H, m).

Step 2: 4-(4-Iodopyrazol-1-yl)-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile

[0333] NMP (2.6 mL) was added to 3-fluoro-4-(4-iodopyrazol-1-yl)benzonitrile (201 mg, 0.642 mmol), 2-methyl-5-phenyl-4H-pyrazol-3-one (123 mg, 0.706 mmol), and potassium carbonate (177 mg, 1.28 mmol), and the mixture was stirred at 120°C overnight. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (198 mg, 66%).
MS: m/z 468.1 $(M+H)^+$.

Step 3: tert-Butyl 4-[1-[4-cyano-2-(2-methyl-5-phenylpyrazol-3-yl)oxyphenyl]pyrazol-4-yl]-5-oxo-1,4-diazepane-1-carboxylate

[0334] tert-Butyl 5-oxo-1,4-diazepane-1-carboxylate (24 mg, 0.11 mmol), copper(I) iodide (3.7 mg, 0.020 mmol), trans-1,2-cyclohexanediamine (2.2 mg, 0.020 mmol) and tripotassium phosphate (62.7 mg, 0.295 mmol) were added to a solution (0.5 mL) of 4-(4-Iodopyrazol-1-yl)-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile (46 mg, 0.098 mmol) in 1,4-dioxane, and the mixture was stirred at 100°C overnight. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.

Step 4: 3-(2-Methyl-5-phenylpyrazol-3-yl)oxy-4-[4-(7-oxo-1,4-diazepan-1-yl)pyrazol-1-yl]benzonitrile

[0335] The crude product obtained in Step 3 was dissolved in dichloromethane (1 mL), TFA (1 mL) was added to the solution, and the mixture was stirred at room temperature for 2 hours. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (15.7 mg).

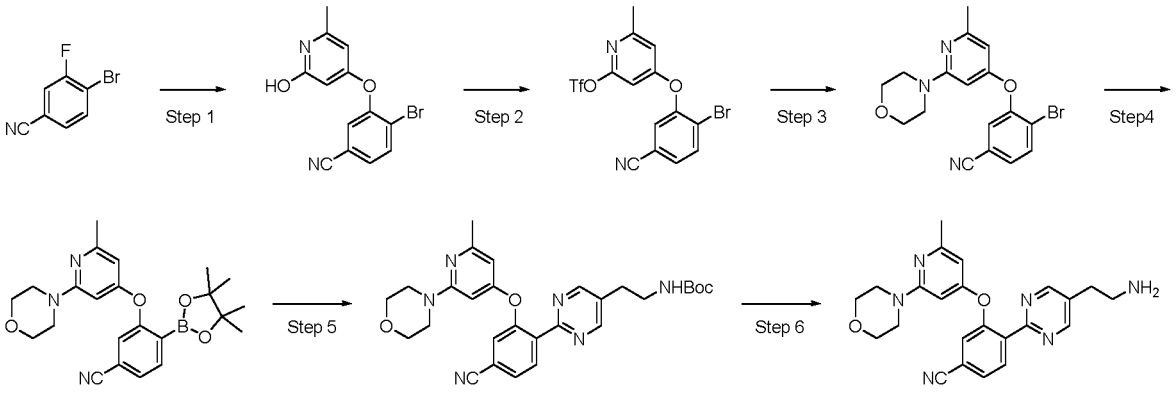
Exact MS: 453.2
Obs. MS $(M+H)^+$: 454.3

[Example 16]

4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile (Compound No. 250)

[0336]

[Chem. 62]



Step 1: 4-Bromo-3-(2-hydroxy-6-methylpyridin-4-yl)oxybenzonitrile

[0337] NMP (400 mL) was added to 4-bromo-3-fluorobenzonitrile (40.0 g, 200 mmol), 6-methylpyridine-2,4-diol (30.0 g, 240 mmol), and sodium carbonate (53.0 g, 500 mmol), and the mixture was stirred at 160°C for 5 hours. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. Ethyl acetate was added to the concentrated crude product to prepare a suspension, heptane was further added to the suspension, and the precipitated solid was collected by filtration through a glass filter. The solid was vacuum dried to obtain the target compound (20.3 g, 33%).

MS: m/z 305.0 $(M+H)^+$.
^{1}H-NMR ($DMSO\text{-}d_6$) δ: 11.47 (1H, s), 8.00 (1H, d, J = 8.2 Hz), 7.92 (1H, d, J = 1.8 Hz), 7.73 (1H, dd, J = 8.2, 2.3 Hz), 5.89 (1H, d, J = 1.8 Hz), 5.15 (1H, d, J = 2.7 Hz), 2.15 (3H, s).

Step 2: [4-(2-Bromo-5-cyanophenoxy)-6-methylpyridin-2-yl]trifluoromethanesulfonate

[0338] Dichloromethane (22 mL) was added to 4-bromo-3-(2-hydroxy-6-methylpyridin-4-yl)oxybenzonitrile (2.7 g, 8.85 mmol), the mixture was cooled to 0°C, and then trifluoromethanesulfonic anhydride (3.25 g, 11.5 mmol) was added to the mixture. Pyridine (2.1 mL, 26.5 mmol) was added dropwise to this reaction mixture at the same temperature, then the temperature was raised to room temperature, and the mixture was stirred for 2 hours. Water was added to the reaction mixture, and the mixture was extracted with dichloromethane. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.
MS: m/z 436.9 $(M+H)^+$.

Step 3: 4-Bromo-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile

[0339] The crude product obtained in Step 2 was dissolved in DMSO (18 mL), then to the solution, morpholine (1.16 g, 13.3 mmol) and N, N-diisopropylethylamine (4.73 mL, 26.5 mmol) were added, and the mixture was stirred at 70°C for 2 hours. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. Ethanol was added to the concentrated crude product and dried overnight. The precipitated target compound was collected by filtration through a glass filter and dried to obtain the target compound (1.87 g, 57%).

MS: m/z 374.0 $(M+H)^+$.
^{1}H-NMR ($CDCl_3$) δ: 7.77 (1H, d, J = 8.2 Hz), 7.35 (1H, dd, J = 8.2, 1.8 Hz), 7.29 (1H, d, J = 1.8 Hz), 6.02 (1H, d, J = 1.4 Hz), 6.00 (1H, d, J = 1.4 Hz), 3.80 (4H, t, J = 5.0 Hz), 3.48 (4H, t, J = 4.8 Hz), 2.36 (3H, s).

Step 4: 3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxy-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile

[0340] 4-Bromo-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile (790 mg, 2.11 mmol) was dissolved in 1,4-dioxane (11 mL), then to the solution, bis(pinacolato)diboron (804 mg, 3.17 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride (76.4 mg, 0.106 mmol), and potassium acetate (415 mg, 4.22 mmol) were added, and the mixture was stirred at 90°C overnight. The reaction mixture was cooled to room temperature, water was added to the

mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (567 mg).
MS: m/z 422.3 $(M+H)^+$.

Step 5: tert-Butyl N-[2-[2-[4-cyano-2-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxyphenyl]pyrimidin-5-yl]ethyl]carbamate

[0341] 3-(2-Methyl-6-morpholin-4-ylpyridin-4-yl)oxy-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (222 mg, 0.527 mmol) was dissolved in 1,4-dioxane (1.8 mL), then to the solution, tert-butyl N-[2-(2-chloropyrimidin-5-yl)ethyl]carbamate (90.5 mg, 0.351 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride (12.8 mg, 0.0176 mmol), potassium carbonate (97.1 mg, 0.702 mmol), and water (0.4 mL) were added, and the mixture was stirred at 90°C overnight. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (71.9 mg, 40%).

MS: m/z 517.3 $(M+H)^+$.
^{1}H-NMR ($CDCl_3$) δ: 8.61 (2H, s), 8.05 (1H, d, J = 8.2 Hz), 7.61 (1H, dd, J = 8.2, 1.4 Hz), 7.44 (1H, d, J = 1.4 Hz), 6.01 (1H, d, J = 1.4 Hz), 5.94 (1H, d, J = 1.8 Hz), 4.70 (1H, brs), 3.78 (4H, t, J = 4.8 Hz), 3.41 (4H, t, J = 4.8 Hz), 3.36 (2H, q, J = 6.6 Hz), 2.82 (2H, t, J = 6.6 Hz), 2.29 (3H, s), 1.43 (9H, s).

Step 6: 4-[5-(2-Aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile

[0342] tert-Butyl N-[2-[2-[4-cyano-2-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxyphenyl]pyrimidin-5-yl]ethyl]carbamate (71. 9 mg, 0.139 mmol) was dissolved in dichloromethane (1 mL), then TFA (1 mL) was added to the solution, and the mixture was stirred at room temperature for 1 hour. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (63.62 mg).

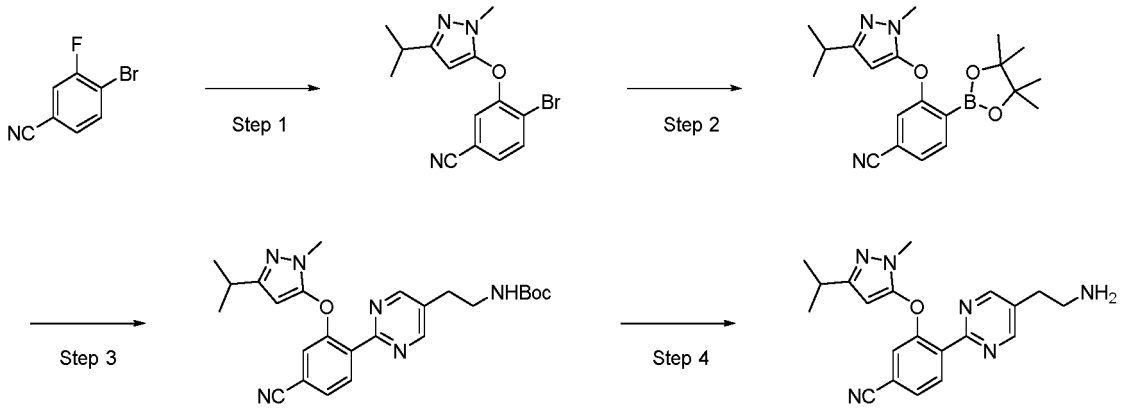
Exact MS: 416.2
Obs. MS $(M+H)^+$: 417.4
^{1}H-NMR (CD_3OD) δ: 8.79 (2H, s), 8.33 (1H, d, J = 8.2 Hz), 7.90 (1H, dd, J = 8.0, 1.6 Hz), 7.79 (1H, d, J = 1.4 Hz), 6.46 (1H, d, J = 1.8 Hz), 6.39 (1H, d, J = 1.8 Hz), 3.79 (4H, t, J = 5.0 Hz), 3.55 (4H, t, J = 5.0 Hz), 3.25 (2H, t, J = 7.8 Hz), 3.04 (2H, t, J = 7.8 Hz), 2.50 (3H, s).

[Example 17]

4-[5-(2-Aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxybenzonitrile (Compound No. 261)

[0343]

[Chem. 63]



Step 1: 4-Bromo-3-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxybenzonitrile

[0344] 4-Bromo-3-fluorobenzonitrile (2.14 g, 10.7 mmol) and 2-methyl-5-propan-2-ylpyrazole-3-ol (1.50 g, 10.7 mmol) were dissolved in DMA (21 mL), then potassium carbonate (4.44 g, 32.1 mmol) was added to the solution, and the mixture was stirred at 130°C for 3 hours. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (1.06 g, 31%).

MS: m/z 322.1 $(M+H)^+$.
^{1}H-NMR ($CDCl_3$) δ: 7.77 (1H, d, J = 8.2 Hz), 7.34-7.32 (2H, m), 5.52 (1H, s), 3.70 (3H, s), 2.94-2.87 (1H, m), 1.25 (6H, d, J = 6.9 Hz).

Step 2: 3-(2-Methyl-5-propan-2-ylpyrazol-3-yl)oxy-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile

[0345] 4-Bromo-3-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxybenzonitrile (646 mg, 2.02 mmol) was dissolved in 1,4-dioxane (10 mL), then to the solution, bis(pinacolato)diboron (615 mg, 2.42 mmol), bis(triphenylphosphine)palladium dichloride (70.8 mg, 0.101 mmol) and potassium acetate (396 mg, 4.03 mmol) were added, and the mixture was stirred at 100°C for 2 hours. The reaction solution was cooled to room temperature and filtered through Celite, and then the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.
MS: m/z 368.2 $(M+H)^+$.

Step 3: tert-Butyl N-[2-[2-[4-cyano-2-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxyphenyl]pyrimidin-5-yl]ethyl]carbamate

[0346] To a solution (13.5 mL) of the crude product in 1,4-dioxane obtained in Step 2, tert-butyl N-[2-(2-chloropyrimidin-5-yl)ethyl]carbamate (520 mg, 2.02 mmol), tetrakis(triphenylphosphine)palladium (117 mg, 0.101 mmol), potassium carbonate (697 mg, 5.04 mmol) and water (3.4 mL) were added, and the mixture was stirred at 100°C for 2 hours. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (946 mg, containing impurities). MS: m/z 463.2 $(M+H)^+$.

Step 4: 4-[5-(2-Aminoethyl)pynmidin-2-yl]-3-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxybenzonitrile

[0347] tert-Butyl N-[2-[2-[4-cyano-2-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxyphenyl]pyrimidin-5-yl]ethyl]carbamate (946 mg, 1.23 mmol) was dissolved in 1,4-dioxane (5.1 mL), then to the solution, a 4 M hydrochloric acid/1,4-dioxane solution (5.1 mL) was added dropwise at 0°C, the temperature of the mixture was raised to room temperature, and the mixture was stirred for 5 hours. The reaction mixture was concentrated under reduced pressure, ethyl acetate was added to the concentrated crude product, and the mixture was concentrated under reduced pressure again. The mixture was vacuum dried to obtain the hydrochloride salt of the target compound (681 mg, 76%).

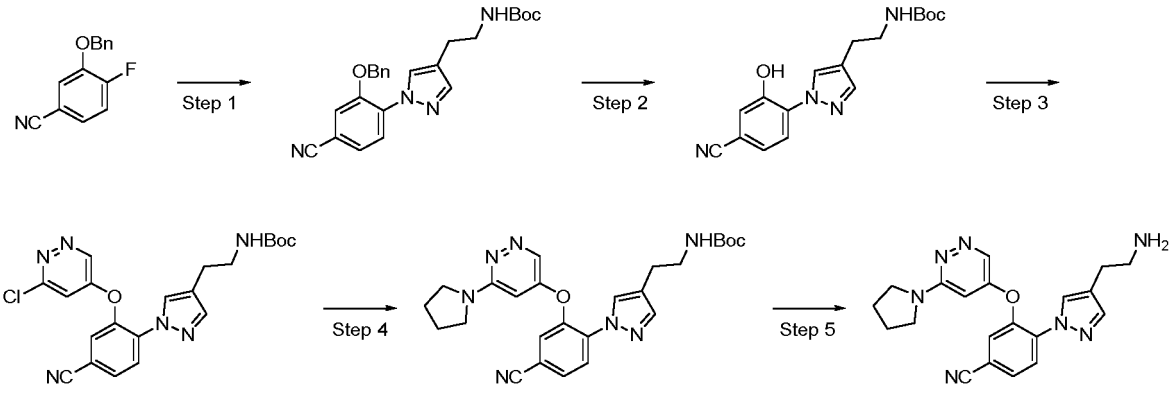
Exact MS: 362.2
Obs. MS $(M+H)^+$: 363.3

[Example 18]

4-[4-(2-Aminoethyl)pyrazol-1-yl]-3-(6-pyrrolidin-1-ylpyridazin-4-yl)oxybenzonitrile (Compound No. 284)

[0348]

[Chem. 64]



Step 1: tert-Butyl N-[2-[1-(4-cyano-2-phenylmethoxyphenyl)pyrazol-4-yl]ethyl]carbamate

[0349] DMA (2 mL) was added to 4-fluoro-3-phenylmethoxybenzonitrile (307 mg, 1.35 mmol), tert-butyl N-[2- (1H-pyrazol-4-yl)ethyl]carbamate (190 mg, 0.900 mmol), and potassium carbonate (373 mg, 2.70 mmol), and the mixture was stirred at 150°C for 2 hours. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (263 mg, 70%).
MS: m/z 419.2 $(M+H)^+$.

Step 2: tert-Butyl N-[2-[1-(4-cyano-2-hydroxyphenyl)pyrazol-4-yl]ethyl]carbamate

[0350] tert-Butyl N-[2-[1-(4-cyano-2-phenylmethoxyphenyl)pyrazol-4-yl]ethyl]carbamate (263 mg, 0.628 mmol) was dissolved in methanol (5 mL)/ethyl acetate (5 mL) and palladium-activated carbon (100 mg) was added to the solution under a nitrogen atmosphere. A hydrogen gas balloon was attached to the reaction vessel, and after the inside of the vessel was replaced with hydrogen gas, the mixture was stirred at room temperature for 30 minutes. The reaction mixture was filtered through Celite, the filtrate was concentrated under reduced pressure, and the crude product was purified by silica gel column chromatography to obtain the target compound (172 mg, 83%).
MS: m/z 273.0 $(M-tBu+H)^+$.

Step 3: tert-Butyl N-[2-[1-[2-(6-chloropyridazin-4-yl)oxy-4-cyanophenyl]pyrazol-4-yl]ethyl]carbamate

[0351] DMF (1.3 mL) was added to tert-butyl N-[2-[1-(4-cyano-2-hydroxyphenyl)pyrazol-4-yl]ethyl]carbamate (172 mg, 0.524 mmol), 3,5-dichloropyridazine (101 mg, 0.681 mmol), and potassium carbonate (217 mg, 1.57 mmol), and the mixture was stirred at 100°C for 1 hour. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (218 mg, 94%).
MS: m/z 385.0 $(M-tBu+H)^+$.

Step 4: tert-Butyl N-[2-[1-[4-cyano-2-(6-pyrrolidin-1-ylpyridazin-4-yl)oxyphenyl]pyrazol-4-yl]ethyl]carbamate

[0352] tert-Butyl N-[2-[1-[2-(6-chloropyridazin-4-yl)oxy-4-cyanophenyl]pyrazol-4-yl]ethyl]carbamate (70.0 mg, 0.159 mmol) was dissolved in toluene (0.8 mL), then to the solution, pyrrolidine (33.9 mg, 0.476 mmol), tris(dibenzylideneacetone)dipalladium (7.3 mg, 7.9 μmol), (±)-BINAP (9.9 mg, 16 μmol)), and cesium carbonate (220 mg, 2.25 mmol) were added, and the mixture was stirred at 100°C for 1 hour. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (51.0 mg, 68%).

Step 5: 4-[4-(2-Aminoethyl)pyrazol-1-yl]-3-(6-pyrrolidin-1-ylpyridazin-4-yl)oxybenzonitrile

[0353] tert-Butyl N-[2-[1-[4-cyano-2-(6-pyrrolidin-1-ylpyridazin-4-yl)oxyphenyl]pyrazol-4-yl]ethyl]carbamate (51.0 mg, 0.107 mmol) was dissolved in dichloromethane (2 mL), then TFA (0.5 mL) was added to the solution, and the mixture

was stirred at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (9.71 mg).

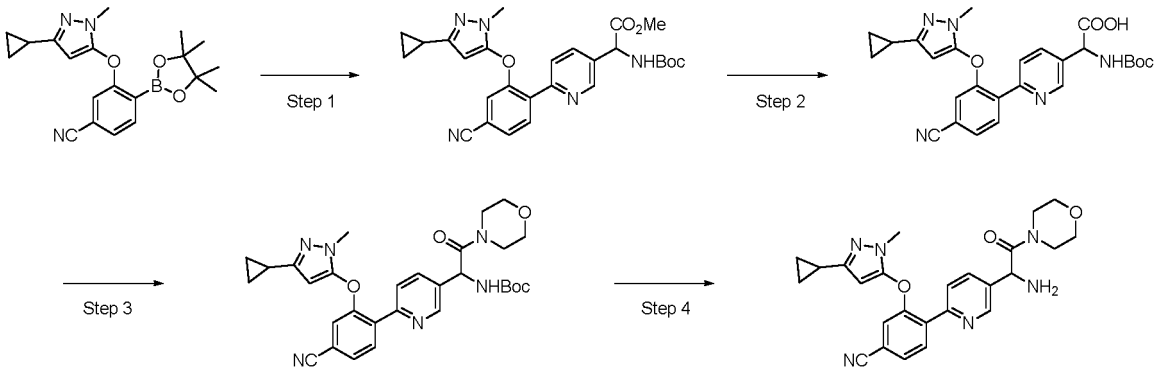
Exact MS: 375.2
Obs. MS $(M+H)^+$: 376.2

[Example 19]

4-[5-(1-Amino-2-morpholin-4-yl-2-oxoethyl)pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile (Compound No. 487)

[0354]

[Chem. 65]



Step 1: Methyl 2-[6-[4-cyano-2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxyphenyl]pyridin-3-yl]-2-[(2-methylpropan-2-yl)oxycarbonylamino]acetate

[0355] 3-(5-Cyclopropyl-2-methylpyrazol-3-yl)oxy-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (881 mg, 2.41 mmol) synthesized in the same method as in Example 17 was dissolved in 1,4-dioxane (12 mL), then to the solution, methyl 2-(6-chloropyridin-3-yl)-2-[(2-methylpropan-2-yl)oxycarbonylamino]acetate (725 mg, 2.41 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride (176.5 mg, 0.241 mmol), potassium carbonate (1.00 g, 7.24 mmol) and water (3 mL) were added, and the mixture was stirred at 100°C for 2 hours. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (976 mg, 80%).
MS: m/z 504.4 $(M+H)^+$.

Step 2: 2-[6-[4-Cyano-2-(5 -cyclopropyl-2-methylpyrazol-3 -yl)oxyphenyl]pyridin-3 - yl]-2-[(2-methylpropan-2-yl)oxycarbonylamino]acetic acid

[0356] Methyl 2-[6-[4-cyano-2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxyphenyl]pyridin-3-yl]-2-[(2-methylpropan-2-yl)oxycarbonylamino]acetate (976 mg, 1.94 mmol) was dissolved in methanol (10 mL), then a 2 M aqueous sodium hydroxide solution (2 mL) was added to the solution, and the mixture was stirred at room temperature for 15 minutes. After adding 1 M hydrochloric acid (4 mL) to the reaction mixture and stirring the mixture, the mixture was extracted by adding ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The crude product was used in the next reaction without further purification.
MS: m/z 490.3 $(M+H)^+$.

Step 3: tert-Butyl N-[1-[6-[4-cyano-2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxyphenyl]pyridin-3-yl]-2-morpholin-4-yl-2-oxoethyl]carbamate

[0357] An aliquot (160 mg, 0.320 mmol) of the crude product obtained in Step 2 was dissolved in DMF (1 mL), then

to the solution, morpholine (0.041 mL, 0.48 mmol), HATU (160 mg, 0.420 mmol), and triethylamine (0.130 mL, 0.960 mmol) were added, and the mixture was stirred at room temperature for 3 hours. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.
MS: m/z 559.4 $(M+H)^+$.

Step 4: 4-[5-(1-Amino-2-morpholin-4-yl-2-oxoethyl)pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile

[0358] The crude product obtained in Step 3 was dissolved in dichloromethane (1 mL), then TFA (0.5 mL) was added to the solution, and the mixture was stirred at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (39.7 mg).

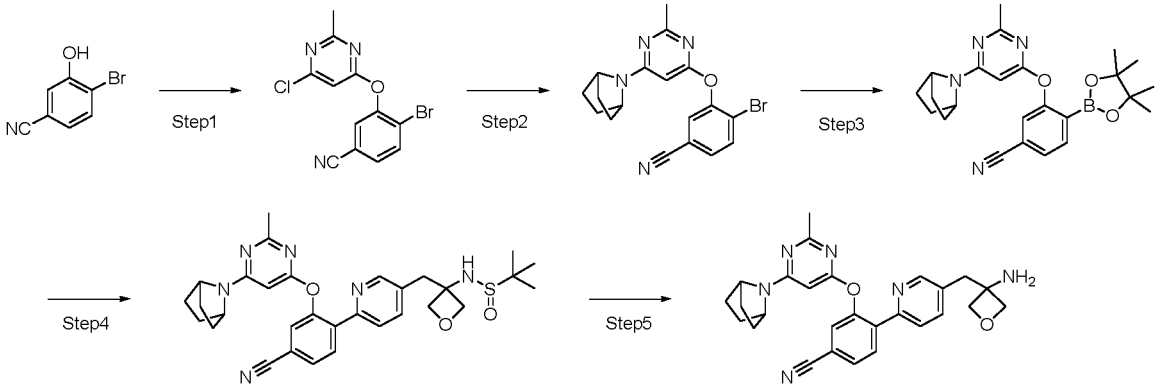
Exact MS: 458.2
Obs. MS $(M+H)^+$: 459.3

[Example 20]

4-[5-[(3-Aminooxetan-3-yl)methyl]pyridin-2-yl]-3-[6-(7-azabicyclo[2.2.1]heptan-7-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile (Compound No. 670)

[0359]

[Chem. 66]



Step 1: 4-Bromo-3-(6-chloro-2-methylpyrimidin-4-yl)oxybenzonitrile

[0360] 4-Bromo-3-hydroxybenzonitrile (1.78 g, 9.00 mmol) was dissolved in DMSO (30 mL), then to the solution, 4,6-dichloro-2-methylpyrimidine (1.28 g, 6.0 mmol) and potassium carbonate (2.49 g, 18.0 mmol) were added, and the mixture was stirred at 80°C overnight. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (1.16 g, 60%).
MS: m/z 324.0 $(M+H)^+$.

Step 2: 3-[6-(7-azabicyclo[2.2.1]heptan-7-yl)-2-methylpyrimidin-4-yl]oxy-4-bromobenzonitrile

[0361] 4-Bromo-3-(6-chloro-2-methylpyrimidin-4-yl)oxybenzonitrile (325 mg, 1.00 mmol) was dissolved in DMF (5 mL), then to the solution, 7-azabicyclo[2.2.1]heptane hydrochloride (200 mg, 1.50 mmol) and potassium carbonate (415 mg, 3.00 mmol) were added, and the mixture was stirred at 80°C overnight. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with a mixed solution of ethyl acetate/heptane (=1/1). The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (235 mg, 61%).

MS: m/z 385.1 $(M+H)^+$.
^{1}H-NMR ($CDCl_3$) δ: 7.73 (1H, d, J = 8.2 Hz), 7.47 (1H, d, J = 2.3 Hz), 7.36 (1H, dd, J = 8.2, 1.8 Hz), 5.89 (1H, s), 4.51 (2H, brs), 2.36 (3H, s), 1.82-1.80 (4H, m), 1.57-1.50 (4H, m).

Step 3: 3-[6-(7-Azabicyclo[2.2.1]heptan-7-yl)-2-methylpyrimidin-4-yl]oxy-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile

[0362] 3-[6-(7-Azabicyclo[2.2.1]heptan-7-yl)-2-methylpyrimidin-4-yl]oxy-4-bromobenzonitrile (231 mg, 0.600 mmol) was dissolved in 1,4-dioxane (3 mL), then to the solution, bis(pinacolato)diboron (305 mg, 1.20 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride (43.9 mg, 0.0600 mmol), and potassium acetate (177 mg, 1.80 mmol) were added, and the mixture was stirred at 100°C overnight. The reaction solution was cooled to room temperature and filtered through Celite, and then the solution was concentrated under reduced pressure. The concentrated crude product was used in the next reaction without further purification.

Step 4: N-[3-[[6-[2-[6-(7-Azabicyclo[2.2.1]heptan-7-yl)-2-methylpyrimidin-4-yl]oxy-4-cyanophenyl]pyridin-3-yl]methyl]oxetan-3-yl]-2-methylpropane-2-sulfinamide

[0363] An aliquot (64.8 mg) of the crude product obtained in Step 3 was dissolved in 1,4-dioxane (1 mL), then to the solution, N-[3-[(6-chloropyridin-3-yl)methyl]oxetan-3-yl]-2-methylpropane-2-sulfinamide (30.3 mg, 0.100 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride (7.3 mg, 0.010 mmol), potassium carbonate (41.5 mg, 0.300 mmol) and water (0.2 mL) were added, and the mixture was stirred at 100°C overnight. The reaction solution was cooled to room temperature and filtered through Celite, and then the solution was concentrated under reduced pressure. The concentrated crude product was used in the next reaction without further purification.

Step 5: 4-[5-[(3-Aminooxetan-3-yl)methyl]pyridin-2-yl]-3-[6-(7-azabicyclo[2.2.1]heptan-7-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile

[0364] The crude product obtained in Step 4 was dissolved in methanol (1 mL), then to the solution, a 4 M hydrochloric acid/1,4-dioxane solution (0.15 mL) was added at 0°C, and the mixture was stirred at the same temperature for 2 hours. Saturated aqueous sodium hydrogen carbonate (5 mL) was added to the reaction mixture, and the mixture was extracted with dichloromethane. The organic layer was dried over anhydrous sodium sulfate and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (8.2 mg).

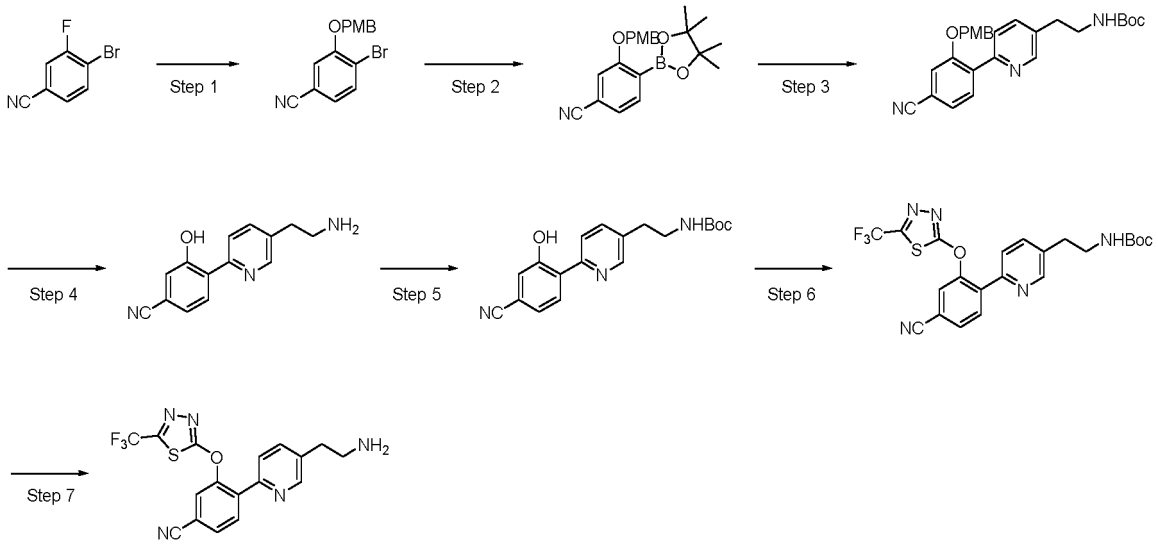
Exact MS: 468.2
Obs. MS $(M+H)^+$: 469.2

[Example 21]

4-[5-(2-Aminoethyl)pyridin-2-yl]-3-[[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]oxy]benzonitrile (Compound No. 712)

[0365]

[Chem. 67]



Step 1: 4-Bromo-3-[(4-methoxyphenyl)methoxy]benzonitrile

[0366] 4-Bromo-3-fluorobenzonitrile (6.00 g, 30.0 mmol) was added to a solution of 4-methoxybenzyl alcohol (4.97 g, 36.0 mmol) and potassium tert-butoxide (4.04 g, 36.0 mmol) in DMF (100 mL), and the mixture was stirred at room temperature for 2.5 hours. Water was added to the reaction mixture, the mixture was stirred, and the precipitated solid was collected by filtration through a glass filter and vacuum dried to obtain the target compound (8.04 g, 84%).
^{1}H-NMR ($CDCl_3$) δ: 7.65 (1H, d, J = 7.8 Hz), 7.37 (2H, d, J = 8.7 Hz), 7.13 (2H, dd, J = 9.8, 1.1 Hz), 6.93 (2H, d, J = 8.2 Hz), 5.11 (2H, s), 3.83 (3H, s).

Step 2: 3-[(4-Methoxyphenyl)methoxy]-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile

[0367] 4-Bromo-3-[(4-methoxyphenyl)methoxy]benzonitrile (1.0 g, 3.14 mmol) was dissolved in 1,4-dioxane (16 mL), then to the solution, bis(pinacolato)diboron (1.20 g, 4.71 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride (115 mg, 0.157 mmol) and potassium acetate (617 mg, 6.29 mmol) were added, and the mixture was stirred at 100°C for 2 hours. The reaction mixture was cooled to room temperature, filtered through Celite, and then concentrated under reduced pressure. The concentrated crude product was used in the next reaction without further purification.
MS: m/z 433.2 $(M+H)^+$.

Step 3: tert-Butyl N-[2-[6-[4-cyano-2-[(4-methoxyphenyl)methoxy]phenyl]pyridin-3-yl]ethyl]carbamate

[0368] tert-Butyl N-[2-(6-chloropyridin-3-yl)ethyl]carbamate (807 mg, 3.14 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride (231 mg, 0.314 mmol), potassium carbonate (2.05 g, 6.29 mmol) and water (1 mL) were added to a solution of the crude product in 1,4-dioxane (6 mL) obtained in Step 2, and the mixture was stirred at 100°C for 4 hours. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (1.17 g, 81%).
MS: m/z 460.2 $(M+H)^+$.

Step 4: 4-[5-(2-Aminoethyl)pyridin-2-yl]-3-hydroxybenzonitrile

[0369] tert-Butyl N-[2-[6-[4-cyano-2-[(4-methoxyphenyl)methoxy]phenyl]pyridin-3-yl]ethyl]carbamate (1.05 g, 1.60 mmol) was dissolved in dichloromethane (10 mL), then TFA (2 mL) was added to the solution, and the mixture was stirred at room temperature for 2 hours. The reaction solution was concentrated under reduced pressure, and the concentrated crude product was used in the next reaction without further purification.

Step 5: tert-Butyl N-[2-[6-(4-cyano-2-hydroxyphenyl)pyridin-3-yl]ethyl]carbamate

[0370] The crude product obtained in Step 4 was dissolved in dichloromethane (5 mL), then to the solution, di-tert-butyl dicarbonate (698 mg, 3.20 mmol) and triethylamine (1.00 mL) were added, and the mixture was stirred at room temperature for 1 hour. Water was added to the reaction mixture, and the mixture was extracted with dichloromethane. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (526 mg, 97%).
MS: m/z 340.1 $(M+H)^+$.

Step 6: tert-Butyl N-[2-[6-[4-cyano-2-[[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]oxy]phenyl]pyridin-3-yl]ethyl]carbamate

[0371] tert-Butyl N-[2-[6-(4-cyano-2-hydroxyphenyl)pyridin-3-yl]ethyl]carbamate (30 mg, 0.088 mmol) was dissolved in NMP (1 mL), then to the solution, 2-bromo-5-(trifluoromethyl)-1,3,4-thiadiazole (24.7 mg, 0.106 mmol) and potassium carbonate (36.7 mg, 0.265 mmol) were added, and the mixture was stirred at 80°C for 1 hour. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The obtained crude product was used in the next reaction without further purification.
MS: m/z 492.1 $(M+H)^+$.

Step 7: 4-[5-(2-Aminoethyl)pyridin-2-yl]-3-[[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]oxy]benzonitrile

[0372] The crude product obtained in Step 6 was dissolved in dichloromethane (1 mL), TFA (0.5 mL) was added to the solution, and the mixture was stirred at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (35.9 mg).

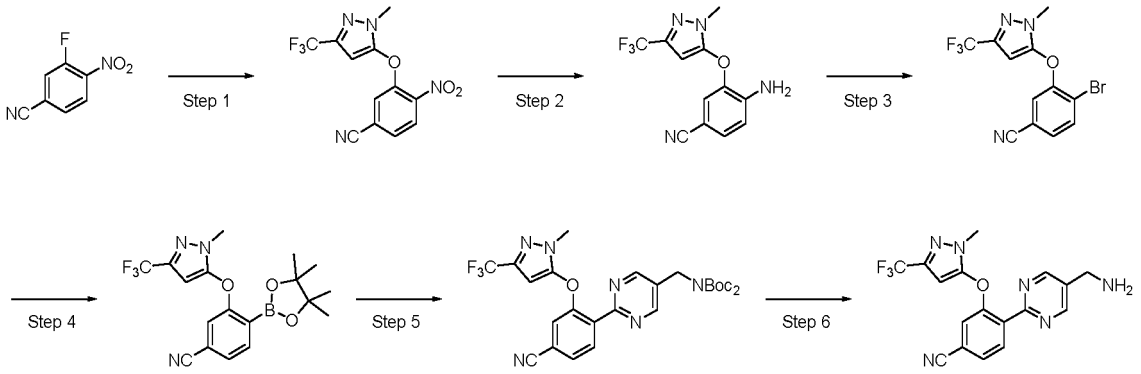
Exact MS: 391.1
Obs. MS $(M+H)^+$: 392.2

[Example 22]

4-[5-(Aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(trifluoromethyl)pyrazol-3-yl]oxybenzonitrile (Compound No. 811)

[0373]

[Chem. 68]



Step 1: 3-[2-methyl-5-(trifluoromethyl)pyrazol-3-yl]oxy-4-nitrobenzonitrile

[0374] 3-Fluoro-4-nitrobenzonitrile (664 mg, 4.00 mmol) and 2-methyl-5-(trifluoromethyl)-4H-pyrazol-3-one (731 mg, 4.40 mmol) were dissolved in DMF (6 mL), then potassium carbonate (663 mg, 4.80 mmol) was added to the solution, and the mixture was stirred at room temperature for 5 hours. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The obtained solid was washed with a small amount of ethyl acetate to obtain the target compound (417 mg).

MS: m/z 313.1 $(M+H)^+$.

Step 2: 4-Amino-3-[2-methyl-5-(trifluoromethyl)pyrazol-3-yl]oxybenzonitrile

[0375] Iron powder (224 mg, 4.01 mmol), ammonium chloride (214 mg, 4.01 mmol), ethanol (1.3 mL) and water (1.3 mL) were added to 3-[2-methyl-5-(trifluoromethyl)pyrazol-3-yl]oxy-4-nitrobenzonitrile (417 mg, 1.34 mmol), and the mixture was stirred at 70°C for 1.5 hours. The reaction mixture was cooled to room temperature, filtered through Celite, and then extracted by adding ethyl acetate and water to the mother liquor. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The concentrated crude product was used in the next reaction without further purification.
MS: m/z 283.1 $(M+H)^+$.

Step 3: 4-Bromo-3-[2-methyl-5-(trifluoromethyl)pyrazol-3-yl]oxybenzonitrile

[0376] The crude product obtained in Step 2 was dissolved in acetonitrile (6.5 mL), then isoamyl nitrite (224 mg, 1.92 mmol) and copper(II) bromide (341 mg, 1.53 mmol) were added to the solution, and the mixture was stirred at 65°C for 16 hours. The reaction mixture was cooled to room temperature, 20% hydrochloric acid was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (389 mg).
MS: m/z 346.0 $(M+H)^+$.

Step 4: 3-[2-Methyl-5-(trifluoromethyl)pyrazol-3-yl]oxy-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile

[0377] 4-Bromo-3-[2-methyl-5-(trifluoromethyl)pyrazol-3-yl]oxybenzonitrile (389 mg, 1.12 mmol) was dissolved in 1,4-dioxane (5.6 mL), then to the solution, bis(pinacolato)diboron (428 mg, 1.68 mmol), bis(triphenylphosphine)palladium dichloride (78.8 mg, 0.112 mmol) and potassium acetate (220 mg, 2.25 mmol) were added, and the mixture was stirred at 110°C for 1 hour. The reaction solution was cooled to room temperature and used in the next reaction without further purification.
MS: m/z 394.2 $(M+H)^+$.

[0378] .

Step 5: tert-Butyl N-[[2-[4-cyano-2-[2-methyl-5-(trifluoromethyl)pyrazol-3-yl]oxyphenyl]pyrimidin-5-yl]methyl]-N-[(2-methylpropan-2-yl)oxycarbonyl]carbamate

[0379] tert-Butyl N-[(2-chloropyrimidin-5-yl)methyl]-N-[(2-methylpropan-2-yl)oxycarbonyl]carbamate (107 mg, 0.31 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride (21 mg, 0.028 mmol), potassium carbonate (120 mg, 0.840 mmol), and water (0.3 mL) were added to an aliquot (1.2 mL) of the reaction mixture obtained in Step 4, and the mixture was stirred at 100°C for 1 hour. The reaction mixture was cooled to room temperature, water was added, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The concentrated crude product was used in the next reaction without further purification.

Step 6: 4-[5-(Aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(trifluoromethyl)pyrazol-3-ylloxybenzonitrile

[0380] Dichloromethane (0.5 mL) and TFA (0.5 mL) were added to the crude product obtained in Step 5, and the mixture was stirred at room temperature for 1 hour. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (88.7 mg).

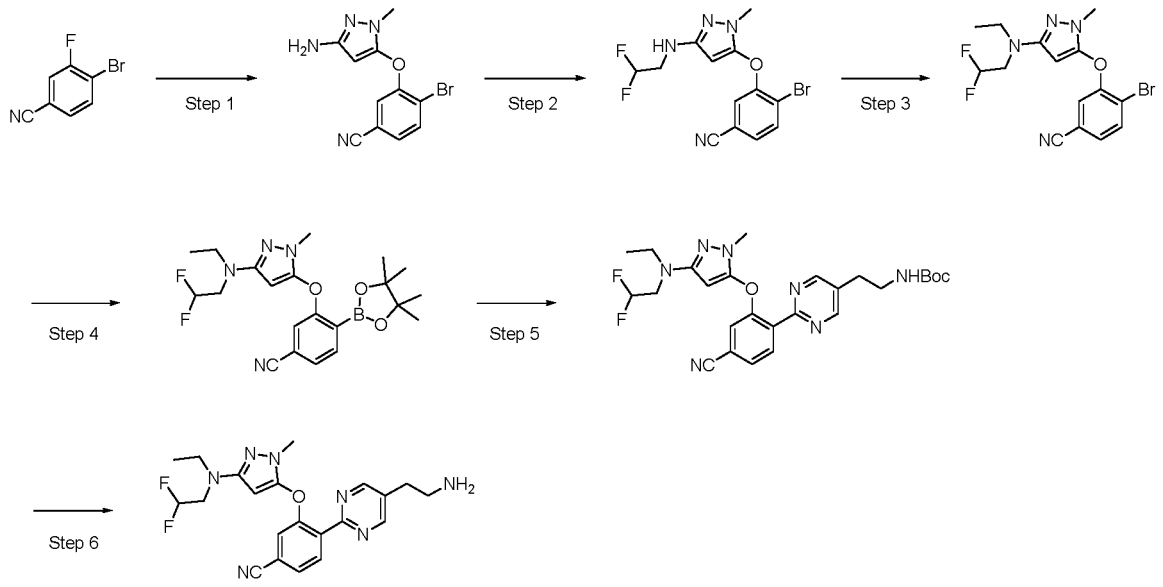
Exact MS: 374.1
Obs. MS $(M+H)^+$: 375.3

[Example 23]

4-[5-(2-Aminoethyl)pyrimidin-2-yl]-3-[5-[2,2-difluoroethyl(ethyl)amino]-2-methylpyrazol-3-yl]oxybenzonitrile (Compound No. 875)

[0381]

[Chem. 69]



Step 1: 3-(5-Amino-2-methylpyrazol-3-yl)oxy-4-bromobenzonitrile

[0382] 4-Bromo-3-fluorobenzonitrile (3.0 g, 15 mmol) and 5-amino-2-methyl-4H-pyrazol-3-one (1.7 g, 15 mmol) were dissolved in DMA (40 mL), and potassium carbonate (4.14 g, 30.0 mmol) was added to the solution, and the mixture was stirred at 120°C for 2 hours. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (444 mg, 10%).

MS: m/z 292.9 $(M+H)^+$.
^{1}H-NMR ($CDCl_3$) δ: 7.76 (1H, d, J = 8.2 Hz), 7.36 (1H, d, J = 1.8 Hz), 7.32 (1H, dd, J = 8.0, 1.6 Hz), 5.11 (1H, s), 3.63 (2H, brs), 3.57 (3H, s).

Step 2: 4-Bromo-3-[5-(2,2-difluoroethylamino)-2-methylpyrazol-3-yl]oxybenzonitrile

[0383] 3-(5-Amino-2-methylpyrazol-3-yl)oxy-4-bromobenzonitrile (1.47 g, 5.00 mmol) was dissolved in DMA (10 mL), then to the solution, 1,1-difluoro-2-iodoethane (1.44 g, 7.50 mmol) and N,N-diisopropylethylamine (1.74 mL, 10.0 mmol) were added, and the mixture was stirred at 140°C overnight. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (1.10 g, 62%).
MS: m/z 359.0 $(M+H)^+$.

Step 3: 4-Bromo-3-[5-[2,2-difluoroethyl(ethyl)aminol-2-methylpyrazol-3-yl]oxybenzonitrile

[0384] 4-Bromo-3-[5-(2,2-difluoroethylamino)-2-methylpyrazol-3-yl]oxybenzonitrile (1.10 g, 3.09 mmol) was dissolved in DMA (10 mL), then to the solution, iodoethane (963 mg, 6.17 mmol) and N,N-diisopropylethylamine (1.08 mL, 6.17 mmol) were added, and the mixture was stirred at 120°C overnight. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (766 mg, 64%).
MS: m/z 385.0 $(M+H)^+$.

Step 4: 3-[5-[2,2-Difluoroethyl(ethyl)amino]-2-methylpyrazol-3-yl]oxy-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile

[0385] 4-Bromo-3-[5-[2,2-difluoroethyl(ethyl)amino]-2-methylpyrazol-3-yl]oxybenzonitrile (766 mg, 1.99 mmol) was dissolved in 1,4-dioxane (10 mL), then to the solution, bis(pinacolato)diboron (758 mg, 2.98 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride (72.8 mg, 0.0995 mmol), and potassium acetate (391 mg, 3.98 mmol) were added, and the mixture was stirred at 100°C for 2 hours. The reaction mixture was cooled to room temperature, filtered through Celite, and then the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.
MS: m/z 433.2 $(M+H)^+$.

Step 5: tert-Butyl N-[2-[2-[4-cyano-2-[5-[2,2-difhioroethyl(ethyl)amino]-2-methylpyrazol-3-yl]oxyphenyl]pyrimidin-5-yl]ethyl]carbamate

[0386] The crude product obtained in Step 4 was dissolved in 1,4-dioxane (10 mL), then to the solution, tert-butyl N-[2-(2-chloropyrimidin-5-yl)ethyl]carbamate (462 mg, 1.79 mmol), tetrakis(triphenylphosphine)palladium (115 mg, 0.0995 mmol), potassium carbonate (550 mg, 3.98 mmol) and water (3 mL) were added, and the mixture was stirred at 100°C for 1 hour. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (648 mg, 62%).
MS: m/z 528.2 $(M+H)^+$.

Step 6: 4-[5-(2-Aminoethyl)pyrimidin-2-yl]-3-[5-[2,2-difluoroethyl(ethyl)amino]-2-methylpyrazol-3-yl]oxybenzonitrile

[0387] tert-Butyl N-[2-[2-[4-cyano-2-[5-[2,2-difluoroethyl(ethyl)amino]-2-methylpyrazol-3-yl]oxyphenyl]pyrimidin-5-yl]ethyl]carbamate (648 mg, 1.23 mmol) was dissolved in 1,4-dioxane (4 mL), then a 4 M hydrochloric acid/1,4-dioxane solution (2 mL) was added dropwise at 0°C to the mixture, then the temperature of the mixture was raised to room temperature, and the mixture was stirred for 2 hours. The reaction mixture was concentrated under reduced pressure, and the solid obtained was vacuum dried to obtain a hydrochloride of the target compound (642 mg).

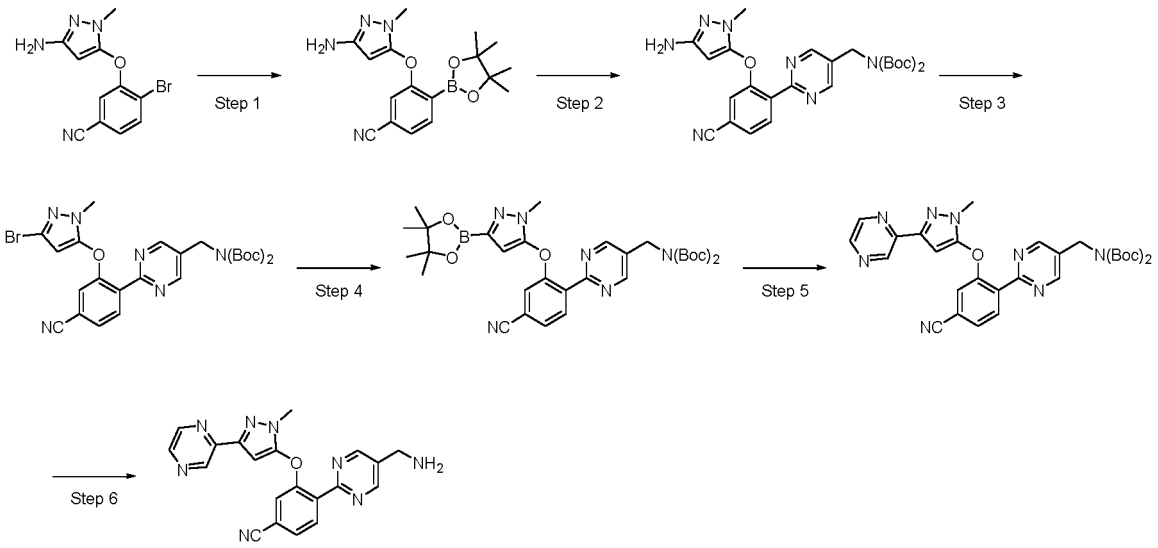
Exact MS: 427.2
Obs. MS $(M+H)^+$: 428.3

[Example 24]

4-[5-(Aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-pyrazin-2-ylpyrazol-3-yl)oxybenzonitrile (Compound No. 931)

[0388]

[Chem. 70]



Step 1 3-(5-Amino-2-methylpyrazol-3-yl)oxy-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile

[0389] The intermediate of 3-(5-amino-2-methylpyrazol-3-yl)oxy-4-bromobenzonitrile (879 mg, 3.00 mmol) obtained in Example 23 was dissolved in 1,4-dioxane (7.5 mL), then to the solution, bis(pinacolato)diboron (1.52 g, 6.00 mmol), bis(triphenylphosphine)palladium dichloride (211 mg, 0.300 mmol), and potassium acetate (589 mg, 6.00 mmol) were added, and the mixture was stirred at 110°C for 2 hours. The reaction mixture was cooled to room temperature, filtered through Celite, and the filtrate was concentrated under reduced pressure. The concentrated crude product was used in the next reaction without further purification.

Step 2: tert-Butyl N-[[2-[2-(5-amino-2-methylpyrazol-3-yl)oxy-4-cyanophenyl]pyrimidin-5-yl]methyl]-N-[(2-methylpropan-2-yl)oxycarbonyl]carbamate

[0390] To a solution of the crude product in 1,4-dioxane (15 mL) obtained in Step 1, tert-butyl N-[(2-chloropyrimidin-5-yl)methyl]-N-[(2-methylpropan-2-yl)oxycarbonyl]carbamate (1.03 g, 3.00 mmol), [1,1'-bis (diphenylphosphino)ferrocene]palladium dichloride (220 mg, 0.300 mmol), potassium carbonate (1.24 g, 9.00 mmol), and water (3 mL) were added, and the mixture was stirred at 100°C for 1 hour. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (1.48 g, containing impurities).
MS: m/z 522.3 $(M+H)^+$.

Step 3: tert-Butyl N-[[2-[2-(5-bromo-2-methylpyrazol-3-yl)oxy-4-cyanophenyl]pynmidin-5-yl]methyl]-N-[(2-methylpropan-2-yl)oxycarbonyl]carbamate

[0391] tert-Butyl N-[[2-[2-(5-amino-2-methylpyrazol-3-yl)oxy-4-cyanophenyl]pyrimidin-5-yl]methyl]-N-[(2-methylpropan-2-yl)oxycarbonyl]carbamate (1.48 g, 2.83 mmol) was dissolved in acetonitrile (28 mL), then isoamyl nitrite (488 mg, 4.17 mmol) and copper(I) bromide (476 mg, 3.32 mmol) were added to the solution, and the mixture was stirred at room temperature overnight. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (289 mg).
MS: m/z 585.2 $(M+H)^+$.

Step 4: tert-Butyl N-[[2-[4-cyano-2-[2-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazol-3-yl]oxyphenyl]pyrimidin-5-yl]methyl]-N-[(2-methylpropan-2-yl)oxycarbonyl]carbamate

[0392] tert-Butyl N-[[2-[2-(5-bromo-2-methylpyrazol-3-yl)oxy-4-cyanophenyl]pyrimidin-5-yl]methyl]-N-[(2-methylpro-

pan-2-yl)oxycarbonyl]carbamate (40 mg, 0.068 mmol) was dissolved in 1,4-dioxane (0.2 mL), then to the solution, bis(pynacolato)diboron (26.0 mg, 0.102 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride (5.0 mg, 6.8 μmol) and potassium acetate (20.1 mg, 0.205 mmol) were added, and the mixture was stirred at 110°C for 2 hours. The reaction mixture was cooled to room temperature, filtered through Celite, and then concentrated under reduced pressure. The crude product obtained was used in the next reaction without further purification.

Step 5: tert-Butyl N-[[2-[4-cyano-2-(2-methyl-5-pyrazin-2-ylpyrazol-3-yl)oxyphenyl]pyrimidin-5-yl]methyl]-N-[(2-methyl-propan-2-yl)oxycarbonyl]carbamate

[0393] An aliquot (24 mg) of the crude product obtained in Step 4 was dissolved in 1,4-dioxane (0.19 mL), then to the solution, 2-chloropyrazine (25.7 mg, 0.076 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride (2.8 mg, 3.8 μmol), potassium carbonate (16 mg, 0.11 mmol) and water (0.038 mL) were added, and the mixture was stirred at 100°C for 1 hour. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.

Step 6: 4-[5-(Aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-pyrazin-2-ylpyrazol-3-yl)oxybenzonitrile

[0394] TFA (0.5 mL) was added to the crude product obtained in Step 5, and the mixture was stirred at room temperature for 1 hour. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (5.25 mg).

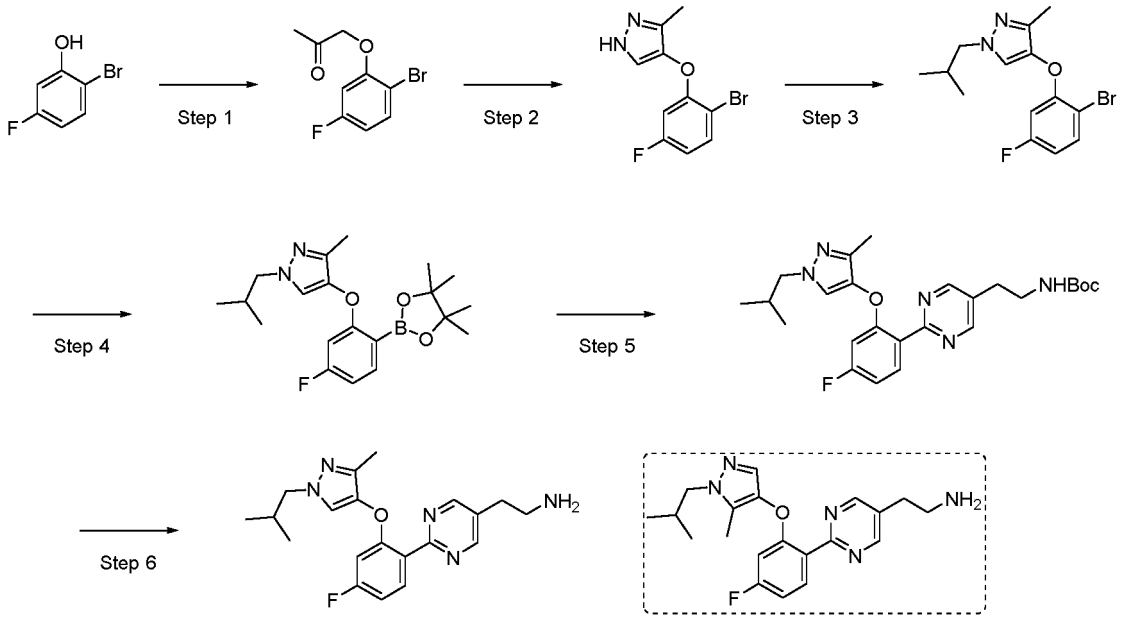
Exact MS: 384.1
Obs. MS $(M+H)^+$: 385.2

[Example 25]

2-[2-[4-Fluoro-2-[3-methyl-1-(2-methylpropyl)pyrazol-4-yl]oxyphenyl]pyrimidin-5-yl]ethanamine (Compound No. 966) (Target compound) and 2-[2-[4-fluoro-2-[5-methyl-1-(2-methylpropyl)pyrazol-4-yl]oxyphenyl]pyrimidin-5-yl]ethanamine (Compound No. 967) (Regioisomer)

[0395]

[Chem. 71]



Step 1: 1-(2-Bromo-5-fluorophenoxy)propan-2-one

[0396] 2-Bromo-5-fluorophenol (2.29 g, 12.0 mmol) and 1-bromopropan-2-one (1.97 g, 14.4 mmol) were dissolved in DMF (20 mL), potassium carbonate (3.32 g, 24.0 mmol) was added to the solution, and the mixture was heated and stirred at 100°C. After completion of the reaction, the reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (2.51 g, 85%).

Step 2: 3-(2-Bromo-5-fluorophenoxy)-4-(dimethylamino)but-3-en-2-one

[0397] To 1-(2-bromo-5-fluorophenoxy)propan-2-one (2.73 g, 11.0 mmol), N,N-dimethylformamide dimethylacetal (1.58 g, 13.2 mmol) was added, the mixture was stirred at 80°C overnight. After cooling the reaction mixture to room temperature, acetic acid (20 mL) and hydrazine monohydrate (826 mg, 16.5 mmol) were added to the mixture, and the mixture was stirred at 100°C for 3 hours. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated aqueous sodium hydrogen carbonate and saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (2.41 g, 81%).
MS: m/z 271.0 $(M+H)^+$.

Step 3: 4-(2-Bromo-5-fluorophenoxy)-3-methyl-1-(2-methylpropyl)pyrazole

[0398] To 4-(2-bromo-5-fluorophenoxy)-3-methyl-1H-pyrazole (270 mg, 1.0 mmol), DMSO (2 mL), 1-bromo-2-methylpropane (160 mg, 1.2 mmol), and potassium carbonate (280 mg, 2.0 mmol) were added, and the mixture was stirred at 100°C for 5 hours. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain a mixture (185 mg) of the target compound and its regioisomer. Regioisomers were separated by HPLC purification after the last step.

MS: m/z 327.1 $(M+H)^+$.
^{1}H-NMR (DMSO-d_6) δ: 7.80 (1H, s), 7.72 (1H, dd, J = 9.2, 2.8 Hz), 6.93-6.88 (1H, m), 6.60 (1H, dd, J = 10.4, 2.8 Hz), 3.81 (1H, d, J = 7.2 Hz), 2.14-2.07 (1H, m), 1.98 (3H, s), 0.85 (6H, d, J = 6.8 Hz).

Step 4: 4-[5-Fluoro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) phenoxy 1-3-methyl-1-(2-methylpropyl)pyrazole

[0399] The isomer mixture (185 mg, 0.565 mmol) obtained in Step 3 was dissolved in 1,4-dioxane (1.1 mL), then to the solution, bis(pinacolato)diboron (215 mg, 0.848 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride (20.7 mg, 0.0283 mmol) and potassium acetate (111 mg, 1.13 mmol) were added, and the mixture was stirred at 100°C for 2 hours. The reaction mixture was cooled to room temperature, filtered through Celite, and then concentrated under reduced pressure. The crude product was used in the next reaction without further purification.

Step 5: tert-Butyl N-[2-[2-[4-fluoro-2-[3-methyl-1-(2-methylpropyl)pyrazol-4-yl]oxyphenyl]pyrimidin-5-yl]ethyl]carbamate

[0400] An aliquot (106 mg) of the crude product obtained in Step 4 was dissolved in 1,4-dioxane (1 mL), then to the solution, tert-butyl N-[2-(2-chloropyrimidin-5-yl)ethyl]carbamate (87. 6 mg, 0.340 mmol), tetrakis(triphenylphosphine)palladium (16.4 mg, 0.0142 mmol), potassium carbonate (78.3 mg, 0.566 mmol), and water (0.3 mL) were added, and the mixture was stirred at 100°C for 2 hours. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.

Step 6: 2-[2-[4-Fluoro-2-[3-methyl-1-(2-methylpropyl)pyrazol-4-yl]oxyphenyl]pyrimidin-5-yl]ethanamine (Target compound) and 2-[2-[4-fluoro-2-[5-methyl-1-(2-methylpropyl)pyrazol-4-yl]oxyphenyl]pyrimidin-5-yl]ethanamine

(Regioisomer)

[0401] The crude product obtained in Step 5 was dissolved in dichloromethane (1 mL), TFA (0.5 mL) was added to the solution, and the mixture was stirred at room temperature for 1 hour. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (11.82 mg) and its regioisomer (10.77 mg).

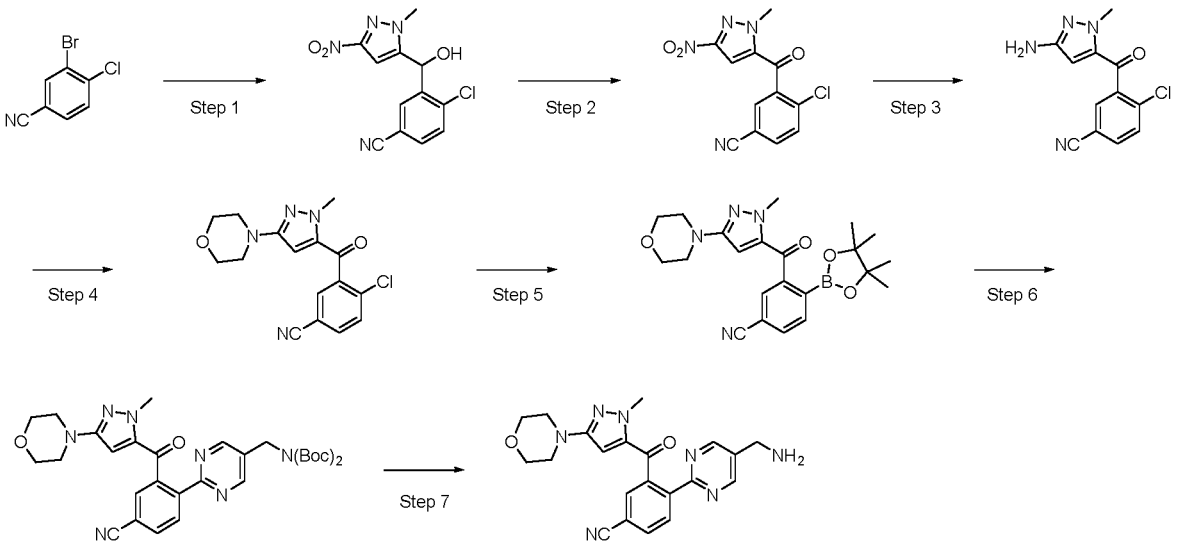
Exact MS: 369.2
Obs. MS $(M+H)^+$: 370.4 (Compound No. 966), 370.3 (Compound No. 967)

[Example 26]

4-[5-(Aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-morpholin-4-ylpyrazole-3-carbonyl)benzonitrile (Compound No. 1028)

[0402]

[Chem. 72]



Step 1: 4-Chloro-3-[hydroxy-(2-methyl-5-nitropyrazol-3-yl)methyl1benzonitrile

[0403] 3-Bromo-4-chlorobenzonitrile (5.69 g, 26.3 mmol) was dissolved in THF (50 mL), then to the solution, isopropylmagnesium chloride lithium chloride complex (14% solution in THF, 20 mL, 26.27 mmol) was added dropwise at 0°C, and the mixture was stirred at the same temperature for 30 minutes. A solution (5 mL) of 2-methyl-5-nitropyrazole-3-carbaldehyde (3.13 g, 20.2 mmol) in THF was added dropwise to this reaction mixture, the temperature of the mixture was raised to room temperature, and the mixture was stirred for 1 hour. 1 M hydrochloric acid was added to the reaction mixture, the mixture was stirred, and then the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (4.85 g, 82%).

MS: m/z 293.1 $(M+H)^+$.
^{1}H-NMR ($CDCl_3$) δ: 8.06 (1H, s), 7.67 (1H, dd, J = 8.2, 1.8 Hz), 7.56 (1H, d, J = 8.2 Hz), 6.39 (1H, s), 6.23 (1H, s), 4.10 (3H, s), 2.97 (1H, s).

Step 2: 4-Chloro-3-(2-methyl-5-nitropyrazole-3-carbonyl)benzonitrile

[0404] Dess-Martin reagent (7.73 g, 18.2 mmol) was added to a solution (83 mL) of 4-chloro-3-[hydroxy-(2-methyl-5-nitropyrazol-3-yl)methyl]benzonitrile (4.85 g, 16.6 mmol) in dichloromethane, and the mixture was stirred at room temperature for 2 hours. A saturated aqueous sodium thiosulfate solution and a saturated aqueous sodium hydrogen carbonate solution were added to the reaction mixture, and the mixture was stirred and then extracted with dichloromethane. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.

MS: m/z 291.0 $(M+H)^+$.
^{1}H-NMR (DMSO-d_6) δ: 8.21 (1H, d, J = 2.3 Hz), 8.11 (1H, dd, J = 8.5, 2.1 Hz), 7.88 (1H, d, J = 8.2 Hz), 7.58 (1H, s), 4.27 (3H, s).

Step 3: 3-(5-Amino-2-methylpyrazole-3-carbonyl)-4-chlorobenzonitrile

[0405] The crude product obtained in Step 2 was suspended in a mixed solvent (66 mL) of ethanol/water (=1/1), then to the suspension, iron powder (2.78 g, 49.7 mmol) and ammonium chloride (2.66 g, 49.74 mol) were added, and the mixture was stirred at 80°C for 2 hours. The reaction mixture was cooled to room temperature and filtered through Celite, and then most of the ethanol was evaporated under reduced pressure. The residue was extracted by adding ethyl acetate, the organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (3.76 g, 87%).

MS: m/z 261.1 $(M+H)^+$.
^{1}H-NMR ($CDCl_3$) δ: 7.72-7.70 (2H, m), 7.60 (1H, d, J = 9.1 Hz), 5.67 (1H, s), 4.11 (3H, s), 3.73 (2H, brs).

Step 4: 4-Chloro-3-(2-methyl-5-morpholin-4-ylpyrazole-3-carbonyl)benzonitrile

[0406] 3-(5-Amino-2-methylpyrazole-3-carbonyl)-4-chlorobenzonitrile (449 mg, 1.72 mmol) was dissolved in NMP (4.3 mL), then to the solution, bis(2-bromoethyl)ether (439 mg, 1.89 mmol) and potassium iodide (28.6 mg, 0.172 mmol) were added, and the mixture was stirred at 110°C for 16 hours. The reaction mixture was cooled to room temperature, ethyl acetate and water were added to the mixture, and the mixture was extracted. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (391 mg, 69%).

MS: m/z 331.1 $(M+H)^+$.
^{1}H-NMR ($CDCl_3$) δ: 7.73-7.71 (2H, m), 7.61 (1H, dd, J = 7.5, 1.6 Hz), 5.68 (1H, s), 4.15 (3H, s), 3.80 (4H, t, J = 4.8 Hz), 3.14 (4H, t, J = 4.8 Hz).

Step 5: 3-(2-Methyl-5-morpholin-4-ylpyrazole-3-carbonyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile

[0407] 4-Chloro-3-(2-methyl-5-morpholin-4-ylpyrazole-3-carbonyl)benzonitrile (391 mg, 1.18 mmol) was dissolved in 1,4-dioxane (4 mL), then to the solution, bis(pinacolato)diboron (451 mg, 1.78 mmol), bis(tricyclohexylphosphine)palladium dichloride (87.3 mg, 0.118 mmol) and potassium acetate (348 mg, 3.55 mmol) were added, and the mixture was stirred at 110°C for 2 hours. The reaction mixture was cooled to room temperature and filtered through Celite, and then the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.
MS: m/z 423.2 $(M+H)^+$.

Step 6: tert-Butyl N-[[2-[4-cyano-2-(2-methyl-5-morpholin-4-ylpyrazole-3-carbonyl)phenyl]pyrimidin-5-yl]methyl]-N-[(2-methylpropan-2-yl)oxycarbonyllcarbamate

[0408] An aliquot (166 mg) of the crude product obtained in Step 5 was dissolved in 1,4-dioxane (1 mL), then to the solution, tert-butyl N-[(2-chloropyrimidin-5-yl)methyl]-N-[(2-methylpropan-2-yl)oxycarbonyl]carbamate (50.0 mg, 0.145 mmol), tetrakis(triphenylphosphine)palladium (16.8 mg, 0.0145 mmol), potassium carbonate (60.3 mg, 0.436 mmol), and water (0.1 mL) were added, and the mixture was stirred at 100°C for 1 hour. The reaction mixture was cooled to room temperature and filtered through Celite, and then the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.

MS: m/z 604.3 $(M+H)^+$.
^{1}H-NMR ($CDCl_3$) δ: 8.70 (2H, s), 8.51 (1H, d, J = 8.2 Hz), 7.90 (1H, d, J = 8.2 Hz), 7.79 (1H, s), 5.38 (1H, S), 4.73 (2H, s), 4.14 (3H, s), 3.72 (4H, t, J = 4.8 Hz), 3.00 (4H, t, J = 4.8 Hz), 1.48 (18H, s).

Step 7: 4-[5-(Aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-morpholin-4-ylpyrazole-3-carbonyl)benzonitrile

[0409] Dichloromethane (1 mL) and TFA (0.5 mL) were added to the crude product obtained in Step 6, and the mixture was stirred at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (34.2 mg).

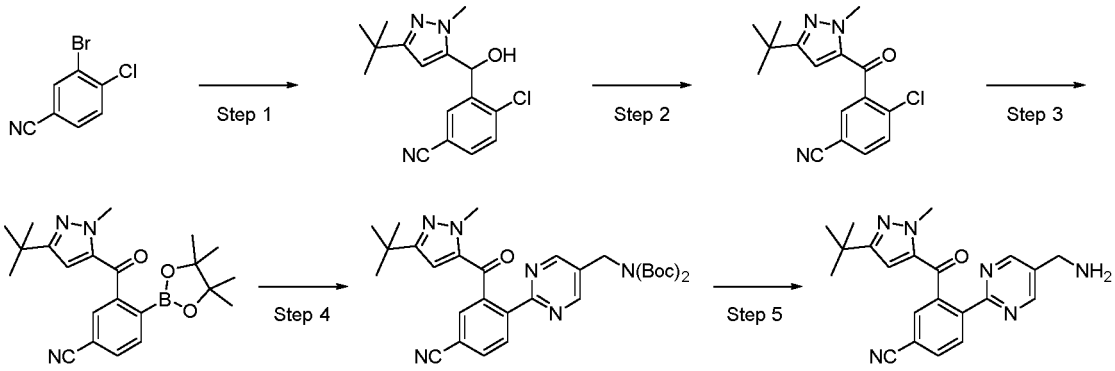
Exact MS: 403.2
Obs. MS $(M+H)^+$: 404.3
^{1}H-NMR (DMSO-d_6) δ: 8.93 (2H, s), 8.49 (1H, d, J = 7.8 Hz), 8.32 (3H, brs), 8.18 (1H, dd, J= 8.2, 1.8 Hz), 8.10 (1H, d, J = 1.8 H), 5.72 (1H, S), 4.10 (2H, d, J = 5.9 Hz), 4.02 (3H, S), 3.57 (4H, t, J = 4.8 Hz), 2.92 (4H, t, J = 4.6 Hz).

[Example 27]

4-[5-(Aminomethyl)pyrimidin-2-yl]-3-(5-tert-butyl-2-methylpyrazole-3-carbonyl)benzonitrile (Compound No. 1030)

[0410]

[Chem. 73]



Step 1: 3-[(5-tert-Butyl-2-methylpyrazol-3-yl)-hydroxymethyl]-4-chlorobenzonitrile

[0411] 3-Bromo-4-chlorobenzonitrile (3.28 g, 15.2 mmol) was dissolved in THF (50 mL), and isopropylmagnesium chloride lithium chloride complex (14% solution in THF, 13 mL, 16.7 mmol) was added dropwise to the solution at 0°C, and the mixture was stirred at the same temperature for 15 minutes. A solution (5 mL) of 5-tert-butyl-2-methylpyrazole-3-carbaldehyde (2.52 g, 15.2 mmol) in THF was added dropwise to the reaction solution, then the temperature of the mixture was raised to room temperature, and the mixture was stirred for 1.5 hours. 1 M Hydrochloric acid was added to the reaction mixture, the mixture was stirred, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. Ethanol was added to the crude product, the mixture was stirred, and then the precipitated solid was collected by filtration through a glass filter, and vacuum dried to obtain the target compound (2.22 g, 48%).

MS: m/z 304.2 $(M+H)^+$.
^{1}H-NMR ($CDCl_3$) δ: 8.02 (1H, d, J = 1.8 Hz), 7.60 (1H, dd, J = 8.2, 1.8 Hz), 7.49 (1H, d, J = 8.2 Hz), 6.15 (1H, d, J = 5.0 Hz), 5.62 (1H, s), 3.90 (3H, s), 2.49 (1H, d, J = 5.0 Hz), 1.23 (9H, s).

Step 2: 3-(5-tert-Butyl-2-methylpyrazole-3-carbonyl)-4-chlorobenzonitrile

[0412] Dess-Martin reagent (768 mg, 1.81 mmol) was added to a solution (16 mL) of 3-[(5-tert-butyl-2-methylpyrazol-3-yl)-hydroxymethyl]-4-chlorobenzonitrile (500 mg, 1.65 mmol) in dichloromethane, and the mixture was stirred at room temperature for 1.5 hours. A saturated aqueous sodium thiosulfate solution and a saturated aqueous sodium hydrogen carbonate solution were added to the reaction mixture, and the mixture was stirred and then extracted with ethyl acetate.

The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (440 mg, 89%).
MS: m/z 302.1 $(M+H)^+$.

Step 3: 3-(5-tert-Butyl-2-methylpyrazole-3-carbonyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile

[0413] 3-(5-tert-Butyl-2-methylpyrazole-3-carbonyl)-4-chlorobenzonitrile (440 mg, 1.46 mmol) was dissolved in 1,4-dioxane (4.9 mL), then to the solution, bis(pinacolato)diboron (556 mg, 2.19 mmol), bis(tricyclohexylphosphine)palladium dichloride (53.9 mg, 0.073 mmol) and potassium acetate (430 mg, 4.38 mmol) were added, and the mixture was stirred at 110°C for 3 hours. The reaction mixture was cooled to room temperature and filtered through Celite, and then the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.
MS: m/z 394.3 $(M+H)^+$.

Step 4: tert-Butyl N-[[2-[2-(5-tert-butyl-2-methylpyrazole-3-carbonyl)-4-cyanophenyl]pynmidin-5-yl]methyl]-N-[(2-methylpropan-2-yl)oxycarbonyl]carbamate

[0414] An aliquot (115 mg) of the crude product obtained in Step 3 was dissolved in 1,4-dioxane (1 mL), then to the solution, tert-butyl N-[(2-chloropyrimidin-5-yl)methyl]-N-[(2-methylpropan-2-yl)oxycarbonyl]carbamate (50.0 mg, 0.145 mmol), tetrakis(triphenylphosphine)palladium (16.8 mg, 0.0145 mmol), potassium carbonate (60.3 mg, 0.436 mmol), and water (0.1 mL) was added, and the mixture was stirred at 100°C for 1 hour. The reaction solution was cooled to room temperature and filtered through Celite, and then the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.
MS: m/z 575.4 $(M+H)^+$.

Step 5: 4-[5-(Aminomethyl)pyrimidin-2-yl]-3-(5-tert-butyl-2-methylpyrazole-3-carbonyl)benzonitrile

[0415] Dichloromethane (1 mL) and TFA (0.5 mL) were added to the crude product obtained in Step 4, and the mixture was stirred at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (9.7 mg).

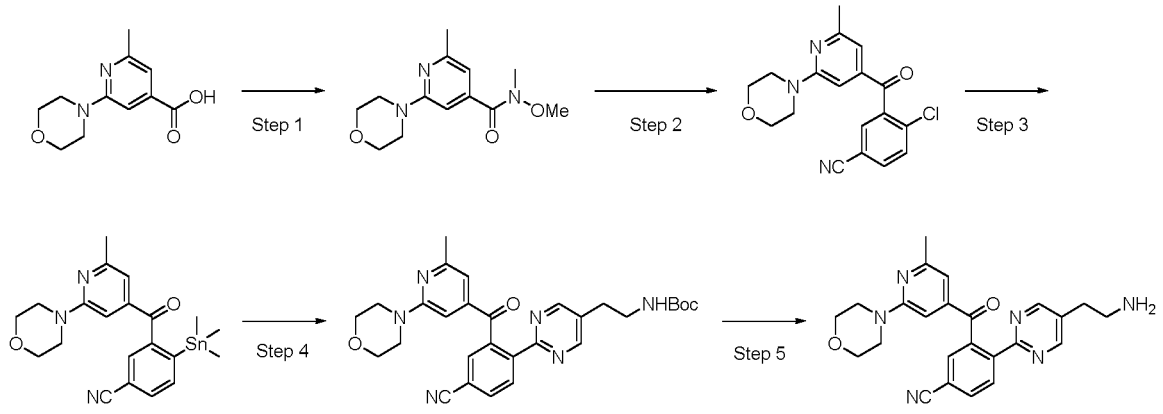
Exact MS: 374.2
Obs. MS $(M+H)^+$: 375.4

[Example 28]

4-[5-(2-Aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridine-4-carbonyl)benzonitrile (Compound No. 1042)

[0416]

[Chem. 74]



Step 1: N-Methoxy-N,2-dimethyl-6-morpholin-4-ylpyridine-4-carboxamide

[0417] 2-Methyl-6-morpholin-4-ylpyridine-4-carboxylic acid (235 mg, 1.43 mmol) was dissolved in DMF (5.3 mL), then to the solution, N,O-dimethylhydroxylamine hydrochloride (124 mg, 1.27 mmol), HATU (524 mg, 1.38 mmol) and triethylamine (0.45 mL, 3.18 mmol) were added, and the mixture was stirred at room temperature for 1 hour. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. The organic layer was dried over anhydrous magnesium sulfate and the solution was concentrated under reduced pressure. Then, the crude product was purified by silica gel column chromatography to obtain the target compound (174 mg, 62%).
MS: m/z 266.1 $(M+H)^+$.

Step 2: 4-Chl oro-3-(2-methyl-6-morpholin-4-ylpyridine-4-carbonyl)benzonitrile

[0418] 3-Bromo-4-chlorobenzonitrile (284 g, 1.31 mmol) was dissolved in THF (3.3 mL), and isopropylmagnesium chloride lithium chloride complex (14% solution in THF, 1.0 mL, 1.31 mmol) was added dropwise to the solution at 0°C, and the mixture was stirred at the same temperature for 30 minutes. A solution (1 mL) of N-methoxy-N,2-dimethyl-6-morpholin-4-ylpyridine-4-carboxamide (174 mg, 0.656 mmol) in THF was added dropwise to the reaction mixture, and then the temperature of the mixture was raised to room temperature, and the mixture was stirred for 1.5 hours. A saturated aqueous ammonium chloride solution was added to the reaction mixture, and the mixture was stirred, and then extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (67.1 mg, 30%).
MS: m/z 342.1 $(M+H)^+$.

Step 3: 3-(2-Methyl-6-morpholin-4-ylpyridine-4-carbonyl)-4-trimethylstannylbenzonitrile

[0419] 4-Chloro-3-(2-methyl-6-morpholin-4-ylpyridine-4-carbonyl)benzonitrile (67.1 mg, 0.196 mmol) was dissolved in 1,4-dioxane (1 mL), then to the solution, hexamethylditin (96.5 mg, 0.294 mmol) and tetrakis(triphenylphosphine)palladium (22.7 mg, 0.0196 mmol) were added, and the mixture was stirred at 110°C for 3 hours. The reaction solution was cooled to room temperature and filtered through Celite, and then the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (21.3 mg, 23%).
MS: m/z 472.1 $(M+H)^+$.

Step 4: tert-Butyl N-[2-[2-[4-cyano-2-(2-methyl-6-morpholin-4-ylpyridine-4-carbonyl)phenyl]pyrimidin-5-yl]ethyl]carbamate

[0420] 3-(2-Methyl-6-morpholin-4-ylpyridine-4-carbonyl)-4-trimethylstannylbenzonitrile (21.3 mg, 0.0453 mmol) was dissolved in 1,4-dioxane (1 mL), then to the solution, tert-butyl N-[2-(2-chloropyrimidin-5-yl)ethyl]carbamate (30.0 mg, 0.116 mmol), tetrakis(triphenylphosphine)palladium (5.2 mg, 4.53 μmol),and copper(I) iodide (1.7 mg, 9.06 μmol) was added, and the mixture was stirred at 110°C for 2 hours. The reaction mixture was cooled to room temperature and filtered through Celite, and then the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.
MS: m/z 529.3 $(M+H)^+$.

Step 5: 4-[5-(2-Aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridine-4-carbonyl)benzonitrile

[0421] Dichloromethane (1.0 mL) and TFA (0.5 mL) were added to the crude product obtained in Step 4, and the mixture was stirred at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (5.0 mg, 26%).

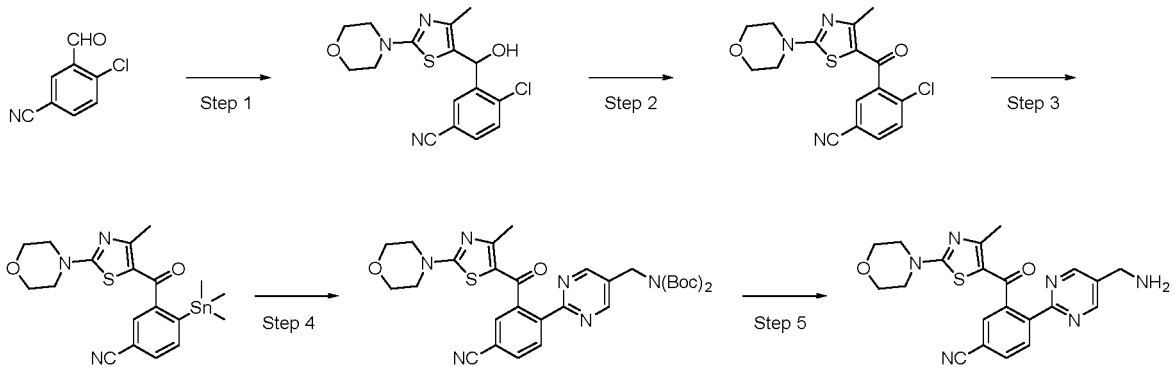
Exact MS: 428.2
Obs. MS ($(M+H)^+$: 429.3

[Example 29]

4-[5-(Aminomethyl)pyrimidin-2-yl]-3-(4-methyl-2-morpholin-4-yl-1,3-thiazole-5-carbonyl)benzonitrile (Compound No. 1064)

[0422]

[Chem. 75]



Step 1: 4-Chloro-3-[hydroxy-(4-methyl-2-morpholin-4-yl-1,3-thiazol-5-yl)methyl]benzonitrile

[0423] 4-(4-Methyl-1,3-thiazol-2-yl)morpholine (1.25 g, 6.78 mmol) was dissolved in THF (34 mL), the solution was cooled to -78°C, then to the solution, an n-butyllithium hexane solution (2.76 M, 2.7 mL, 7.46 mmol) was added dropwise, and the mixture was stirred at the same temperature for 30 minutes. To the reaction mixture, 4-chloro-3-formylbenzonitrile (1.24 g, 7.46 mmol) was added, and the mixture was stirred at -78°C for 1 hour. Then, the temperature of the mixture was raised to room temperature, a saturated aqueous ammonium chloride solution was added to the mixture, the mixture was stirred, and then extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (1.30 g, 55%).
MS: m/z 350.0 $(M+H)^+$.

Step 2: 4-Chloro-3-(4-methyl-2-morpholin-4-yl-1,3-thiazole-5-carbonyl)benzonitrile

[0424] 4-Chloro-3-[hydroxy-(4-methyl-2-morpholin-4-yl-1,3-thiazol-5-yl)methyl]benzonitrile (500 mg, 1.43 mmol) was dissolved in THF (15 mL), then to the solution, 2-iodoxybenzoic acid (801 mg, 2.86 mmol) was added, and the mixture was stirred at 50°C for 2 hours. The reaction mixture was cooled to room temperature, a saturated aqueous sodium thiosulfate solution was added, and the mixture was extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulfate and the solution was concentrated under reduced pressure. Then, the crude product was purified by silica gel column chromatography to obtain the target compound (310 mg, 62%).
MS: m/z 348.0 $(M+H)^+$.

Step 3: 3-(4-Methyl-2-morpholin-4-yl-1,3-thiazole-5-carbonyl)-4-trimethylstannylbenzonitrile

[0425] 4-Chloro-3-(4-methyl-2-morpholin-4-yl-1,3-thiazole-5-carbonyl)benzonitrile (170 mg, 0.489 mmol) was dissolved in 1,4-dioxane (1.2 mL), then to the solution, hexamethylditin (240 mg, 0.733 mmol) and tetrakis(triphenylphosphine)palladium (56.5 mg, 0.0489 mmol) were added, and the mixture was stirred at 110°C for 4 hours. The reaction mixture was cooled to room temperature and purified directly by silica gel column chromatography to obtain the target compound (138 mg, 59%).
MS: m/z 478.0 $(M+H)^+$.

Step 4: tert-Butyl N-[[2-[4-cyano-2-(4-methyl-2-morpholin-4-yl-1,3-thiazole-5-carbonyl)phenyl]pyrimidin-5-yl]methyl]-N-[(2-methylpropan-2-yl)oxycarbonyl]carbamate

[0426] 3-(4-Methyl-2-morpholin-4-yl-1,3-thiazole-5-carbonyl)-4-trimethylstannylbenzonitrile (46.0 mg, 0.0966 mmol) was dissolved in 1,4-dioxane (1 mL), then to the solution, tert-butyl N-[(2-chloropyrimidin-5-yl)methyl]-N-[(2-methylpropan-2-yl)oxycarbonyl]carbamate (66.0 mg, 0.193 mmol), tetrakis(triphenylphosphine)palladium (11.2 mg, 9.66 μmol) and copper(I) iodide (3.68 mg, 0.0193 mmol) were added, and the mixture was stirred at 110°C for 16 hours. The reaction mixture was concentrated under reduced pressure, and the crude product was used in the next reaction without further purification.

Step 5: 4-[5-(Aminomethyl)pyrimidin-2-yl]-3-(4-methyl-2-morpholin-4-yl-1,3-thiazole-5-carbonyl)benzonitrile

[0427] Dichloromethane (0.5 mL) and TFA (0.5 mL) were added to the crude product obtained in Step 4, and the mixture was stirred at room temperature for 2 hours. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (10.8 mg).

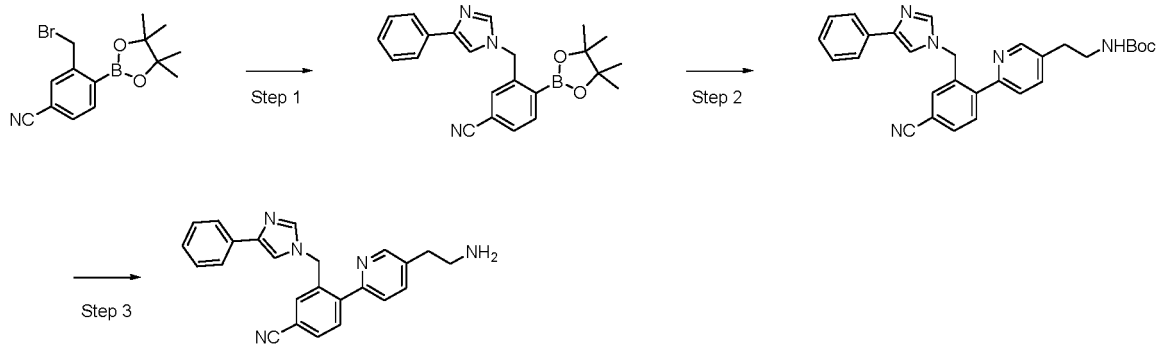
Exact MS: 420.1
Obs. MS $(M+H)^+$: 421.2

[Example 30]

4-[5-(2-Aminoethyl)pyridin-2-yl]-3-[(4-phenylimidazol-1-yl)methyl]benzonitrile (Compound No. 1131)

[0428]

[Chem. 76]



Step 1: 3-[(4-Phenylimidazol-1-yl)methyll-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile

[0429] 3-(Bromomethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (6.00 g, 18.6 mmol) was dissolved in DMF (80 mL), then to the solution, 4-phenyl-1H-imidazole (2.69 g, 18.6 mmol) and potassium carbonate (5.15 g, 37.3 mmol) were added, and the mixture was stirred at 80°C for 3 hours. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The obtained crude product was used in the next reaction without further purification.
MS: m/z 386.2 $(M+H)^+$.

Step 2: tert-Butyl N-[2-[6-[4-cyano-2-[(4-phenylimidazol-1-yl)methyl]phenyl]pyridin-3- yl]ethyl]carbamate

[0430] The crude product obtained in Step 1 was dissolved in 1,4-dioxane (80 mL), then to the solution, tert-butyl N-[2-(6-chloropyridin-3-yl)ethyl]carbamate (3.87 g, 15.1 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride (552 mg, 0.754 mmol), potassium carbonate (4.17 g, 30.2 mmol) and water (20 mL) were added, and the mixture was stirred at 100°C for 2 hours. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The extract was dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (1.41 g, 20%).
MS: m/z 480.2 $(M+H)^+$.

Step 3: 4-[5-(2-Aminoethyl)pyridin-2-yl]-3-[(4-phenylimidazol-1-yl)methyl]benzonitrile

[0431] 1,4-Dioxane (20 mL) was added to tert-butyl N-[2-[6-[4-cyano-2-[(4-phenylimidazol-1-yl)methyl]phenyl]pyridin-3-yl]ethyl]carbamate (1.19 g, 2.49 mmol), then to the mixture, a 4 M hydrochloric acid/dioxane solution (20 mL) was added dropwise at 0°C, the temperature of the mixture was raised to room temperature, and the mixture was stirred for 3 hours. The reaction solution was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (678 mg, 72%).

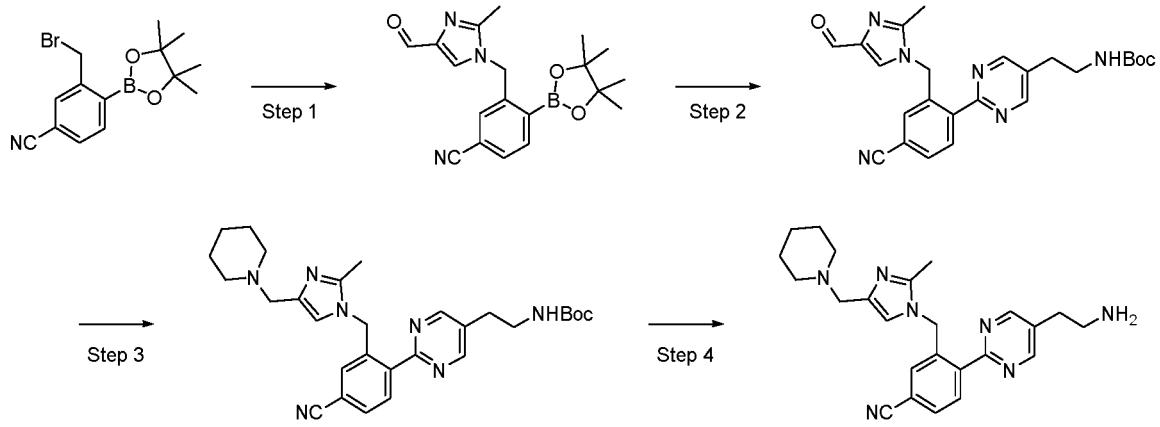
Exact MS: 379.2
Obs. MS $(M+H)^+$: 380.3

[Example 31]

4-[5-(2-Aminoethyl)pyrimidin-2-yl]-3-[[2-methyl-4-(piperidin-1-ylmethyl)imidazol-1-yl]methyl]benzonitrile (Compound No. 1179)

[0432]

[Chem. 77]



Step 1: 3-[(4-Formyl-2-methylimidazol-1-yl)methyl]-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile

[0433] 3-(Bromomethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (354 mg, 1.10 mmol) was dissolved in acetonitrile (5 mL), then to the solution, 2-methyl-1H-imidazole-4-carbaldehyde (110 mg, 1.00 mmol) and triethylamine (0.356 mL, 2.00 mmol) were added, and the mixture was stirred at 80°C for 1 hour. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product obtained was used in the next reaction without further purification.

Step 2: tert-Butyl N-[2-[2-[4-cyano-2-[(4-formyl-2-methylimidazol-1-yl)methyl]phenyl]pyrimidin-5-yl]ethyl]carbamate

[0434] The crude product obtained in Step 1 was dissolved in 1,4-dioxane (5 mL), then to the solution, tert-butyl N-[2-(2-chloropyrimidin-5-yl)ethyl]carbamate (283 mg, 1.10 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride (73.4 mg, 0.100 mmol), potassium carbonate (415 mg, 3.00 mmol) and water (1 mL) were added, and the mixture was stirred at 100°C for 1 hour. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The extract was dried over anhydrous sodium sulfate and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (446 mg, quant.).
MS: m/z 447.3 $(M+H)^+$.

Step 3: tert-Butyl N-[2-[2-[4-cyano-2-[[2-methyl-4-(piperidin-1-ylmethyl)imidazol-1-yl]methyl]phenyl]pyrimidin-5-yl]ethyl]carbamate

[0435] tert-Butyl N-[2-[2-[4-cyano-2-[(4-formyl-2-methylimidazol-1-yl)methyl]phenyl]pyrimidin-5-yl]ethyl]carbamate (31. 0 mg, 0.070 mmol) was dissolved in dichloromethane (0.7 mL), then to the solution, piperidine (7.2 mg, 0.084 mmol) and sodium triacetoxyborohydride (37.0 mg, 0.180 mmol) were added, and the mixture was stirred at room temperature for 5 hours. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The obtained crude product was used in the next reaction without further purification.

Step 4: 4-[5-(2-Aminoethyl)pyrimidin-2-yl]-3-[[2-methyl-4-(piperidin-1-ylmethyl)imidazol-1-yl]methyl]benzonitrile

[0436] Dichloromethane (0.5 mL) and TFA (0.5 mL) were added to the crude product obtained in Step 3, and the mixture was stirred at room temperature for 1 hour. The mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (12.2 mg).

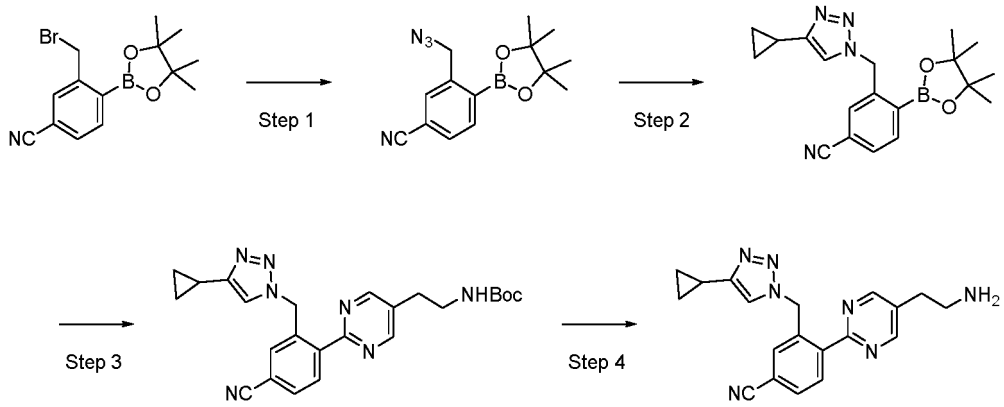
Exact MS: 415.3
Obs. MS $(M+H)^+$: 416.4

[Example 32]

4-[5-(2-Aminoethyl)pyrimidin-2-yl]-3-[(4-cyclopropyltriazol-1-yl)methyl]benzonitrile (Compound No. 1187)

[0437]

[Chem. 78]



Step 1: 3-(Azidomethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile

[0438] 3-(Bromomethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (3.50 g, 10.9 mmol) was dissolved in DMSO (22 mL), then to the solution, sodium azide (777 mg, 12.0 mmol) was added, and the mixture was stirred at 70°C for 3 hours. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (2.80 g, 91%).

Step 2: 3-[(4-Cyclopropyltriazol-1-yl)methyl]-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile

[0439] 3-(Azidomethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (1.10 g, 3.87 mmol) was dissolve in DMSO (10 mL), then to the solution, ethynylcyclopropane (307 mg, 4.65 mmol), copper(I) iodide (36.9 mg, 0.194 mmol) and TBTA (103 mg, 0.194 mmol) were added, and the mixture was stirred at room temperature overnight. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (416 mg, 31%).

Step 3: tert-Butyl N-[2-[2-[4-cyano-2-[(4-cyclopropyltriazol-1-yl)methyl]phenyl]pyrimidin-5-yl]ethyl]carbamate

[0440] 3-[(4-Cyclopropyltriazol-1-yl)methyl]-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (208 mg, 0.594 mmol) was dissolved in 1,4-dioxane (3 mL), then to the solution, tert-butyl N-[2-(2-chloropyrimidin-5-yl)ethyl]carbamate (168 mg, 0.653 mmol), tetrakis(triphenylphosphine)palladium (34 mg, 0.030 mmol), sodium carbonate (126 mg, 1.19 mmol) and water (1 mL) were added, and the mixture was stirred at 80°C overnight. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concen-

trated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (120 mg, 45%.).

Step 4: 4-[5-(2-Aminoethyl)pyrimidin-2-yl]-3-[(4-cyclopropyltriazol-1-yl)methyl]benzonitrile

[0441] Dichloromethane (1 mL) and TFA (0.5 mL) were added to tert-butyl N-[2-[2-[4-cyano-2-[(4-cyclopropyltriazol-1-yl)methyl]phenyl]pyrimidin-5-yl]ethyl]carbamate (120 mg, 0.269 mmol), and the mixture was stirred at room temperature for 1 hour. The mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (12.8 mg).

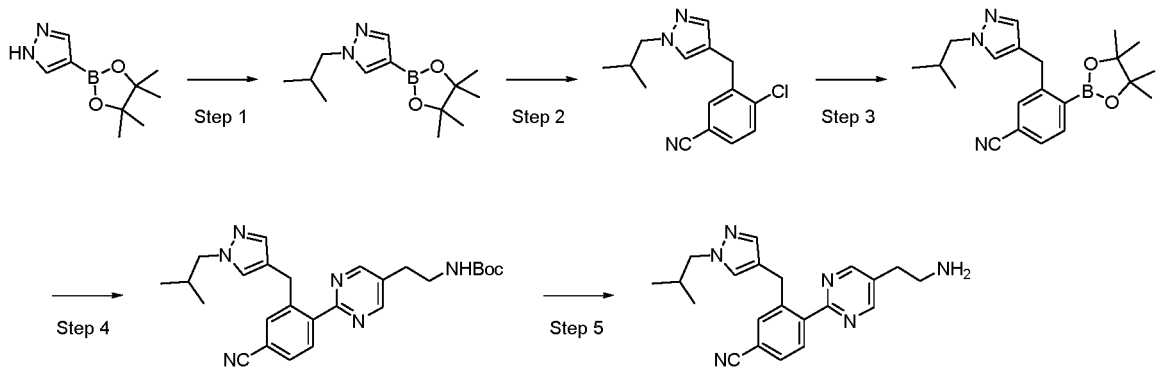
Exact MS: 345.2
Obs. MS $(M+H)^+$: 346.2

[Example 33]

4-[5-(2-Aminoethyl)pyrimidin-2-yl]-3-[[1-(2-methylpropyl)pyrazol-4-yl]methyl]benzonitrile (Compound No. 1195)

[0442]

[Chem. 79]



Step 1: 1-(2-Methylpropyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole

[0443] 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (1.94 g, 10.0 mmol) was dissolved in DMF (10 mL), then to the solution, 1-bromo-2-methylpropane (1.64 g, 12.0 mmol) and potassium carbonate (4.14 g, 30.0 mmol) were added, and the mixture was stirred at 100°C for 2 hours. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The obtained crude product was used in the next reaction without further purification.
MS: m/z 251.2 $(M+H)^+$.

Step 2: 4-Chloro-3-[[1-(2-methylpropyl)pyrazol-4-yl]methyl]benzonitrile

[0444] An aliquot (500 mg, 2.00 mmol) of the crude product obtained in Step 1 was dissolved in 1,4-dioxane (10 mL), then to the solution, 3-(bromomethyl)-4-chlorobenzonitrile (461 mg, 2.00 mmol), tetrakis(triphenylphosphine)palladium (162 mg, 0.140 mmol), cesium carbonate (1.95 g, 6.00 mmol) and water (2 mL) were added, and the mixture was stirred at 100°C overnight. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (548 mg, containing impurities).
MS: m/z 274.1 $(M+H)^+$.

Step 3: 3-[[1-(2-Methylpropyl)pyrazol-4-yl]methyl]-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile

[0445] 4-Chloro-3-[[1-(2-methylpropyl)pyrazol-4-yl]methyl]benzonitrile (274 mg, 1.00 mmol) was dissolved in 1,4-dioxane (3.3 mL), then to the solution, bis(pinacolato)diboron (381 mg, 1.50 mmol), bis(tricyclohexylphosphine)palladium dichloride (73.8 mg, 0.100 mmol), and potassium acetate (294 mg, 3.00 mmol) were added, and the mixture was stirred at 110°C for 2 hours. The reaction mixture was cooled to room temperature, filtered through Celite, and then concentrated under reduced pressure. The crude product was used in the next reaction without further purification.
MS: m/z 366.3 $(M+H)^+$.

Step 4: tert-Butyl N-[2-[2-[4-cyano-2-[[1-(2-methylpropyl)pyrazol-4-yl]methyl]phenyl]pyrimidin-5-yl]ethyl]carbamate

[0446] An aliquot (37 mg) of the crude product obtained in Step 3 was dissolved in 1,4-dioxane (0.5 mL), then to the solution, tert-butyl N-[2-(2-chloropyrimidin-5-yl)ethyl]carbamate (25.8 mg, 0.100 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride (7.3 mg, 0.01 mmol), potassium carbonate (41.0 mg, 0.300 mmol), and water (0.1 mL) were added, and the mixture was stirred at 100°C for 1 hour. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The solution was dried over anhydrous sodium sulfate, the solution was concentrated under reduced pressure, and the crude product was used in the next reaction without further purification.

Step 5: 4-[5-(2-Aminoethyl)pyrimidin-2-yl]-3-[[1-(2-methylpropyl)pyrazol-4-yl]methyl]benzonitrile

[0447] TFA (0.5 mL) was added to the crude product obtained in Step 4, and the mixture was stirred at room temperature for 1 hour. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (26.0 mg).

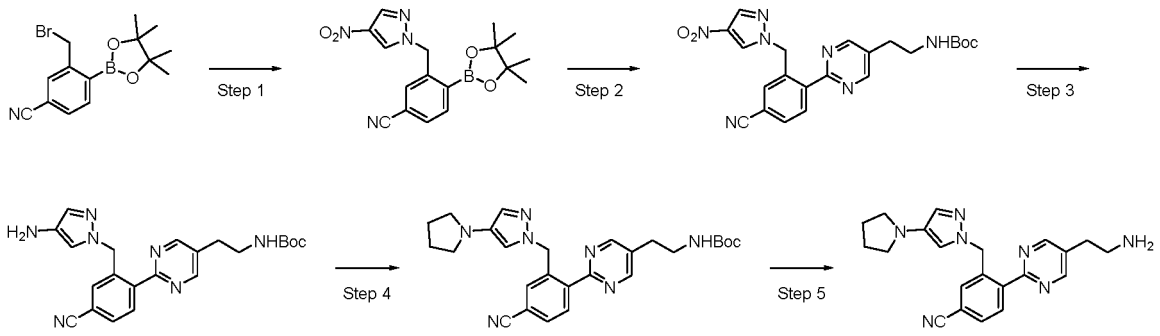
Exact MS: 360.2
Obs. MS $(M+H)^+$: 361.0

[Example 34]

4-[5-(2-Aminoethyl)pyrimidin-2-yl]-3-[(4-pyrrolidin-1-ylpyrazol-1-yl)methyl]benzonitrile (Compound No. 1198)

[0448]

[Chem. 80]



Step 1: 3-[(4-Nitropyrazol-1-yl)methyl]-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile

[0449] 3-(bromomethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (230 mg, 0.700 mmol) was dissolved in DMF (0.7 mL), then to the solution, 4-nitro-1H-pyrazole (95 mg, 0.84 mmol) and potassium carbonate (190 mg, 1.40 mmol) were added, and the mixture was stirred at room temperature for 2 hours. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, the solvent was evaporated under reduced pressure, and the crude product was used in the next reaction without further purification.
MS: m/z 355.2 $(M+H)^+$.

Step 2: tert-Butyl N-[2-[2-[4-cyano-2-[(4-nitropyrazol-1-yl)methyl]phenyl]pyrimidin-5-yl]ethyl]carbamate

[0450] The crude product obtained in Step 1 was dissolved in 1,4-dioxane (3.5 mL), then to the solution, tert-butyl N-[2-(2-chloropyrimidin-5-yl)ethyl]carbamate (180 mg, 0.700 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride (51.2 mg, 0.0700 mmol), potassium carbonate (290 mg, 2.10 mmol), and water (0.7 mL) were added, and the mixture was stirred at 100°C for 1 hours. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The solution was dried over anhydrous sodium sulfate and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (310 mg, 99%).
MS: m/z 450.2 $(M+H)^+$.

Step 3: tert-Butyl N-[2-[2-[2-[(4-aminopyrazol-1-yl)methyl]-4-cyanophenyl]pyrimidin-5-yl]ethyl]carbamate

[0451] tert-Butyl N-[2-[2-[4-cyano-2-[(4-nitropyrazol-1-yl)methyl]phenyl]pyrimidin-5-yl]ethyl]carbamate (310 mg, 0.690 mmol) was dissolved in methanol (0.7 mL) and palladium-active carbon ethylenediamine complex (50 mg) was added to the mixture. A hydrogen gas balloon was attached to the reaction vessel, and after the inside of the vessel was replaced with hydrogen gas, the mixture was stirred at room temperature overnight. After filtering the reaction mixture with Celite, the solution was concentrated under reduced pressure, and the crude product was used in the next reaction without further purification.
MS: m/z 420.3 $(M+H)^+$.

Step 4: tert-Butyl N-[2-[2-[4-cyano-2-[(4-pyrrolidin-1-ylpyrazol-1-yl)methyl]phenyl]pyrimidin-5-yl]ethyl]carbamate

[0452] An aliquot (45.2 mg) of the crude product obtained in Step 3 was dissolved in DMA (0.5 mL), then to the solution, 1,4-dibromobutane (25.6 mg, 0.119 mmol) and N,N-diisopropylethylamine (0.054 mL, 0.323 mmol) were added, and the mixture was stirred at 110°C overnight. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.
MS: m/z 474.3 $(M+H)^+$.

Step 5: 4-[5-(2-Aminoethyl)pyrimidin-2-yl]-3-[(4-pyrrolidin-1-ylpyrazol-1-yl)methyl]benzonitrile

[0453] TFA (0.5 mL) was added to the crude product obtained in Step 4, and the mixture was stirred at room temperature for 1 hour. The mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (7.4 mg).

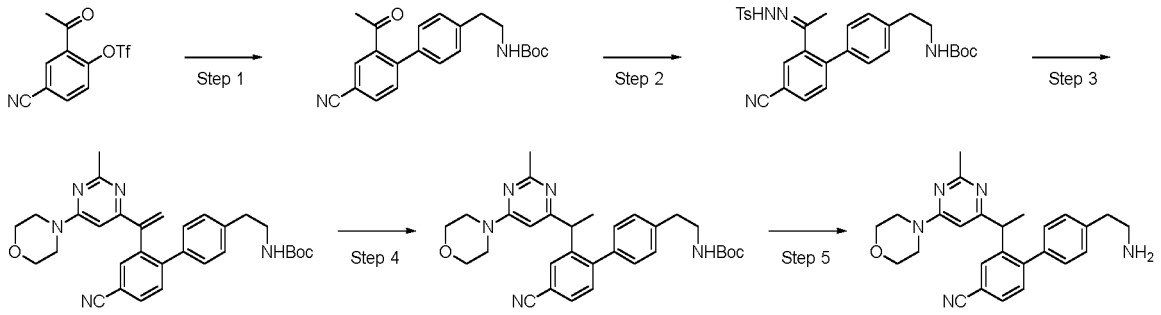
Exact MS: 373.2
Obs. MS $(M+H)^+$: 374.2

[Example 35]

4-[4-(2-Aminoethyl)phenyl]-3-[1-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)ethyl]benzonitrile (Compound No. 1226))

[0454]

[Chem. 81]



Step 1: tert-Butyl (2-(2'-acetyl-4'-cyano-[1,1'-biphenyl]-4-yl)ethyl)carbamate

[0455] To a mixed solution (5 mL) of 2-acetyl-4-cyanophenyltrifluoromethanesulfonate (250 mg, 0.85 mmol) in toluene/water (=4/1), tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaboran-2-yl)phenethylcarbamate (355 mg, 1.02 mmol), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium (62.4 mg, 0.085 mmol), and potassium carbonate (354 mg, 2.56 mmol) were added, and the mixture was stirred at 110°C for 30 minutes. The reaction mixture was cooled to room temperature, and water and ethyl acetate were added to the mixture. The mixture was extracted with ethyl acetate, the organic layer was dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (328 mg, quant.).
MS: m/z 309.1 $(M+H-tBu)^+$.

Step 2: tert-Butyl (2-(4'-cyano-2'-(1-(2-tosylhydrazono)ethyl)-[1,1'-biphenyl]-4-yl)ethyl)carbamate

[0456] p-Toluene sulfonyl hydrazide (167 mg, 0.899 mmol) was added to a solution (3 mL) of tert-butyl (2-(2'-acetyl-4'-cyano-[1,1'-biphenyl]-4-yl)ethyl)carbamate (328 mg, 0.899 mmol) in toluene, and the mixture was stirred at 110°C for 3 hours. The reaction solution was concentrated under reduced pressure, and the crude product was used in the next reaction without further purification.
MS: m/z 477.2 $(M+H-tBu)^+$.

Step 3: tert-Butyl (2-(4'-cyano-2'-(1-(2-methyl-6-morpholinopyrimidin-4-yl)vinyl)-[1,1'-biphenyl1-4-yl)ethyl)carbamate

[0457] The crude product obtained in Step 2 was dissolved in 1,4-dioxane (4.5 mL), then to the solution, 4-(6-chloro-2-methylpyrimidin-4-yl)morpholine (192 mg, 0.899 mmol), tris(dibenzylideneacetone)dipalladium (32.9 mg, 0.036 mmol), 2-(dicyclohexylphosphino)-2',4',6'-tri-i-propyl-1,1'-biphenyl (68.6 mg, 0.14 mmol) and lithium tert-butoxide (166 mg, 2.07 mmol) were added, and the mixture was stirred at 110°C for 3 hours. The reaction mixture was cooled to room temperature and filtered through Celite, and then the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (96.1 mg, 20%).
MS: m/z 526.3 $(M+H)^+$.

Step 4: tert-Butyl (2-(4'-cyano-2'-(1-(2-methyl-6-morpholinopyrimidin-4-yl)ethyl)-[1,1'-biphenyl1-4-yl)ethyl)carbamate

[0458] Ethyl acetate (4 mL) was added to tert-butyl (2-(4'-cyano-2'-(1-(2-methyl-6-morpholinopyrimidin-4-yl)vinyl)-[1,1'-biphenyl]-4-yl)ethyl)carbamate (79 mg, 0.15 mmol), and 10% palladium-activated carbon (20 mg) was added to the mixture under a nitrogen atmosphere. A hydrogen gas balloon was attached to the reaction vessel, the inside of the vessel was replaced with hydrogen gas, and the mixture was stirred at room temperature for 1 hour. After replacing the reaction system with nitrogen, the reaction mixture was filtered through Celite and concentrated under reduced pressure. The obtained crude product was used in the next reaction without further purification.
MS: m/z 528.3 $(M+H)^+$.

Step 5: 4-[4-(2-Aminoethyl)phenyl]-3-[1-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)ethyl]benzonitrile

[0459] The crude product obtained in Step 4 was dissolved in dichloromethane (1 mL), TFA (0.5 mL) was added to the mixture, and the mixture was stirred at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (30.8 mg).

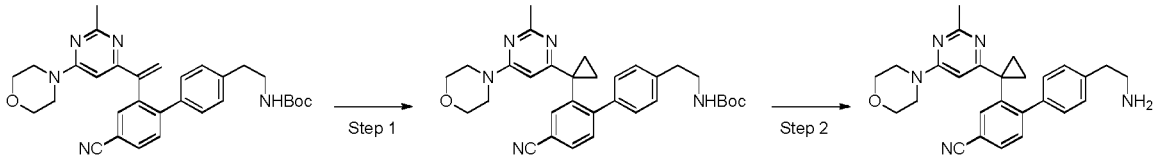
Exact MS: 427.2
Obs. MS $(M+H)^+$: 428.5

[Example 36]

4-[4-(2-Aminoethyl)phenyl]-3-[1-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)cyclopropyl]benzonitrile (Compound No. 1227)

[0460]

[Chem. 82]



Step 1: tert-Butyl (2-(4'-cyano-2'-(1-(2-methyl-6-morpholinopyrimidin-4-yl)cyclopropyl)-[1,1'-biphenyl]-4-yl)ethyl)carbamate

[0461] DMSO (0.5 mL) and sodium hydride (1.3 mg) were added to trimethyl sulfoxonium iodide (7.1 mg, 0.032 mmol), the mixture was stirred at room temperature for 40 minutes, then to the mixture, a solution (0.5 mL) of tert-butyl (2-(4'-cyano-2'-(1-(2-methyl-6-morpholinopyrimidin-4-yl)vinyl)-[1,1'-biphenyl]-4-yl)ethyl)carbamate (16.9 mg, 0.032 mmol) in DMSO obtained in Example 35 was added, and the mixture was stirred at room temperature for 1 hour. Water was added to the reaction mixture, the mixture was extracted with ethyl acetate, and the organic layer was dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The crude product was used in the next reaction without further purification.
MS: m/z 540.3 $(M+H)^+$.

Step 2: 4-[4-(2-Aminoethyl)phenyl]-3-[1-(2-methyl-6-morpholin-4-ylpyrimidin-4-yl)cyclopropyl]benzonitrile

[0462] The crude product obtained in Step 1 was dissolved in dichloromethane (1 mL), TFA (0.5 mL) was added to the solution, and the mixture was stirred at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by silica gel column chromatography to obtain the target compound (11.6 mg).

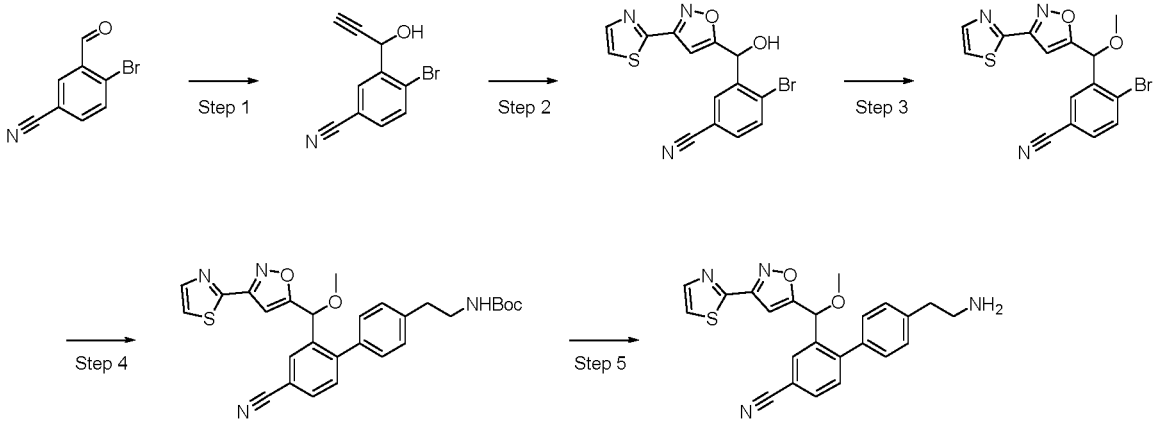
Exact MS: 439.2
Obs. MS $(M+H)^+$: 440.5

[Example 37]

4-[4-(2-Aminoethyl)phenyl]-3-[methoxy-[3-(1,3-thiazol-2-yl)-1,2-oxazol-5-yl]methyl]benzonitrile (Compound No. 1232)

[0463]

[Chem. 83]



Step 1: 4-Bromo-3-(1-hydroxyprop-2-ynyl)benzonitrile

[0464] THF (40 mL) was added to 4-bromo-3-formylbenzonitrile (1.38 g, 6.57 mmol), then to the mixture, a 0.5 M ethynylmagnesium bromide solution (14.5 mL, 7.23 mmol) in THF was added dropwise at 0°C, and the mixture was stirred at the same temperature for 1 hour. After completion of the reaction, 2 M hydrochloric acid was added to the mixture and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product obtained was used in the next reaction.

Step 2: 4-Bromo-3-[hydroxy-[3-(1,3-thiazol-2-yl)-1,2-oxazol-5-yl]methyl]benzonitrile

[0465] To an aliquot (283 mg) of the crude product obtained in Step 1, (2Z) -N-hydroxy-1,3-thiazole-2-carboximidoyl chloride (163 mg, 1.00 mmol), potassium carbonate (276 mg, 2.00 mmol) and toluene (1 mL) were added, and the mixture was stirred at 100°C overnight. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (65.6 mg, 18%).
MS: m/z 362.0 $(M+H)^+$.

Step 3: 4-Bromo-3-[methoxy-[3-(1,3-thiazol-2-yl)-1,2-oxazol-5-yl]methyl]benzonitrile

[0466] 4-Bromo-3-[hydroxy-[3-(1,3-thiazol-2-yl)-1,2-oxazol-5-yl]methyl]benzonitrile (65.6 mg, 0.181 mmol) was dissolved in DMF (1 mL), then sodium hydride (9.5 mg, 0.217 mmol) was added to the mixture, and the mixture was stirred at room temperature for 10 minutes. Iodomethane (38.8 mg, 0.272 mmol) was added to the reaction mixture, and the mixture was stirred at room temperature overnight. After completion of the reaction, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product obtained was used in the next reaction.
MS: m/z 377.9 $(M+H)^+$.

Step 4: tert-Butyl N-[2-[4-[4-cyano-2-[methoxy-[3-(1,3-thiazol-2-yl)-1,2-oxazol-5-yl]methyl]phenyl]phenyl]ethyl]carbamate

[0467] The crude product obtained in Step 3 was dissolved in 1,4-dioxane (0.8 mL), then to the solution, tert-butyl N-[2-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]ethyl]carbamate (75.4 mg, 0.217 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride (6.6 mg, 9.0 μmol), potassium carbonate (50.0 mg, 0.362 mmol) and water (0.2 mL) were added, and the mixture was stirred at 100°C for 1 hour. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The solution was dried over anhydrous sodium sulfate, the solution was concentrated under reduced pressure, and the crude product was used in the next reaction without further purification.
MS: m/z 517.2 $(M+H)^+$.

Step 5: 4-[4-(2-aminoethyl)phenyl]-3-[methoxy-[3-(1,3-thiazol-2-yl)-1,2-oxazol-5-yl]methyl]benzonitrile

[0468] Dichloromethane (1 mL) and TFA (0.5 mL) were added to the crude product obtained in Step 4, and the mixture was stirred at room temperature for 30 minutes. The mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (48.3 mg).

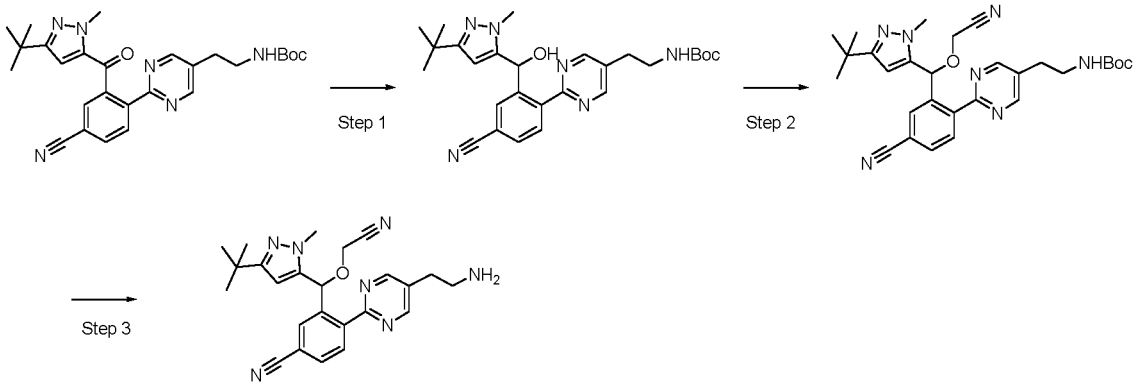
Exact MS: 416.1
Obs. MS $(M+H)^+$: 417.2

[Example 38]

4-[5-(2-Aminoethyl)pyrimidin-2-yl]-3-[(5-tert-butyl-2-methylpyrazol-3-yl)-(cyanomethoxy)methyl]benzonitrile (Compound No. 1237)

[0469]

[Chem. 84]



Step 1: tert-Butyl N-[2-[2-[2-[(5-tert-butyl-2-methylpyrazol-3-yl)-hydroxymethyl]-4-cyanophenyl]pyrimidin-5-yl]ethyl]carbamate

[0470] THF (7.8 mL) was added to tert-butyl N-[2-[2-[2-(5-tert-butyl-2-methylpyrazole-3-carbonyl)-4-cyanophenyl]pyrimidin-5-yl]ethyl]carbamate (379 mg, 0.776 mmol), which can be synthesized in the same method as in Example 27, and a 4 M lithium borohydride solution (0.776 mL, 2.33 mmol) in THF was added dropwise to the mixture. After stirring the mixture at room temperature for 1 hour, water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product obtained was used in the next reaction.
MS: m/z 491.3 $(M+H)^+$.

Step 2: tert-Butyl N-[2-[2-[2-[(5-tert-butyl-2-methylpyrazol-3-yl)-(cyanomethoxy)methyl]-4-cyanophenyl]pyrimidin-5-yl]ethyl]carbamate

[0471] An aliquot (127 mg) of the crude product obtained in Step 1 was dissolved in DMF (1 mL), then to the solution, chloroacetonitrile (23.4 mg, 0.310 mmol) and cesium carbonate (169 mg, 0.517 mmol) were added, and the mixture was stirred at 60°C for 16 hours. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solution was concentrated under reduced pressure. The crude product obtained was used in the next reaction.
MS: m/z 530.3 $(M+H)^+$.

Step 3: 4-[5-(2-Aminoethyl)pyrimidin-2-yll-3-[(5-tert-bulyl-2-methylpyrazol-3-yl)-(cyanomethoxy)methyllbenzonitrile

[0472] Dichloromethane (1 mL) and TFA (0.5 mL) were added to the crude product obtained in Step 2, and the mixture was stirred at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure, and

the crude product was purified by HPLC to obtain the target compound (10.2 mg).

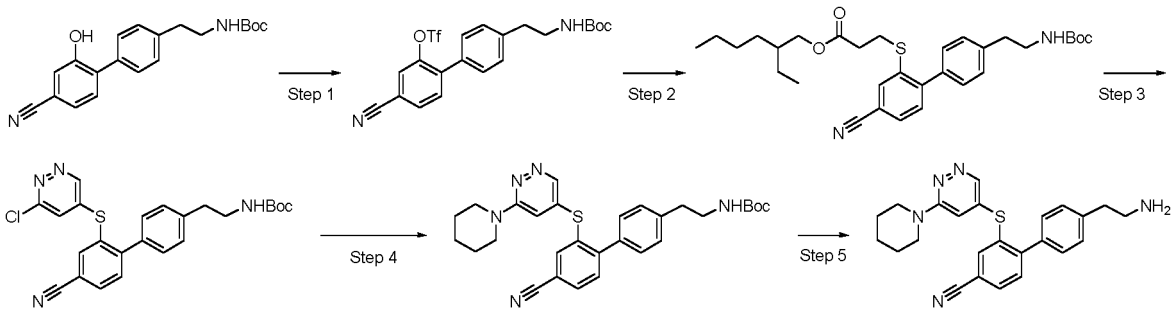
Exact MS: 429.2
Obs. MS $(M+H)^+$: 430.2

[Example 39]

4-[4-(2-Aminoethyl)phenyl]-3-(6-piperidin-1-ylpyridazin-4-yl)sulfanylbenzonitrile (Compound No. 1240)

[0473]

[Chem. 85]



Step 1: [5-Cyano-2-[5-[2-[(2-methylpropan-2-yl)oxycarbonylamino]ethyl]pyridin-2-yllphenylltrifluoromethanesulfonate

[0474] Dichloromethane (5 mL), and pyridine (172 mg, 2.17 mmol) were added to the intermediate of tert-butyl N-[2-[4-(4-cyano-2-hydroxyphenyl)phenyl]ethyl]carbamate (245 mg, 0.724 mmol) obtained in Example 6, the mixture was cooled to 0°C, and trifluoromethanesulfonic anhydride (306 mg, 1.09 mmol) was added dropwise to the mixture. After stirring the mixture at the same temperature for 30 minutes, water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (301 mg, 88%).
MS: m/z 415.0 $(M-tBu+H)^+$.

Step 2: 2-Ethylhexyl 3-[5-cyano-2-[4-[2-[(2-methylpropan-2-yl)oxycarbonylamino]ethyl]phenyl]phenyl]sulfanylpropanoate

[0475] [5-Cyano-2-[5-[2-[(2-methylpropan-2-yl)oxycarbonylamino]ethyl]pyridin-2-yl]phenyl]trifluoromethanesulfonate (301 mg, 0.640 mmol) was dissolved in 1,4-dioxane (2.6 mL), then to the solution, 2-ethylhexyl 3-mercaptopropionate (168 mg, 0.768 mmol), tris(dibenzylideneacetone)dipalladium (29 mg, 0.032 mmol), 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (37 mg, 0.064 mmol) and N,N-diisopropylethylamine (0.223 mL, 1.28 mmol) were added, and the mixture was stirred at 100°C for 2 hours. The reaction mixture was cooled to room temperature, filtered through Celite, and then concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (479 mg, containing impurities).
MS: m/z 439.2 $(M-Boc+H)^+$.

Step 3: tert-Butyl N-[2-[4-[2-(6-chloropyridazin-4-yl)sulfanyl-4-cyanophenyl]phenyl]ethyl]carbamate

[0476] 2-Ethylhexyl 3-[5-cyano-2-[4-[2-[(2-methylpropan-2-yl)oxycarbonylamino]ethyl]phenyl]phenyl]sulfanylpropanoate (479 mg) was dissolved in DMF (5 mL), then to the solution, 3,5-dichloropyridazine (265 mg, 1.78 mmol) and DBU (0.5 mL) were added, and the mixture was stirred at 50°C for 30 minutes. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The solution was dried over anhydrous sodium sulfate and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (340 mg).

MS: m/z 411.0 $(M-tBu+H)^+$.

^{1}H-NMR ($CDCl_3$) δ: 8.58 (1H, d, J = 2.3 Hz), 7.98 (1H, d, J = 1.4 Hz), 7.86 (1H, dd, J = 8.0, 1.6 Hz), 7.61 (1H, d, J = 7.8 Hz), 7.22-7.17 (4H, m), 6.83 (1H, d, J = 2.3 Hz), 4.65 (1H, brs), 3.36 (2H, q, J = 6.6 Hz), 2.80 (2H, t, J = 6.9 Hz), 1.45 (9H, s).

Step 4: tert-Butyl N-[2-[4-[4-cyano-2-(6-piperidin-1-ylpyridazin-4-yl)sulfanylphenyl]phenyl]ethyl]carbamate

[0477] DMF (1 mL) was added to tert-butyl N-[2-[4-[2-(6-chloropyridazin-4-yl)sulfanyl-4-cyanophenyl]phenyl]ethyl]carbamate (50.0 mg, 0.107 mmol), then to the solution, piperidine (27.4 mg, 0.321 mmol) and N,N-diisopropylethylamine (0.15 mL) were added, and the mixture was stirred at 100°C overnight. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The solution was dried over anhydrous sodium sulfate, the solution was concentrated under reduced pressure, and the crude product was used in the next reaction without further purification.

Step 5: 4-[4-(2-Aminoethyl)phenyl]-3-(6-piperidin-1-ylpyridazin-4 - yl)sulfanylbenzonitrile

[0478] Dichloromethane (1 mL) and TFA (0.5 mL) were added to the crude product obtained in Step 4, and the mixture was stirred at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (41.7 mg).

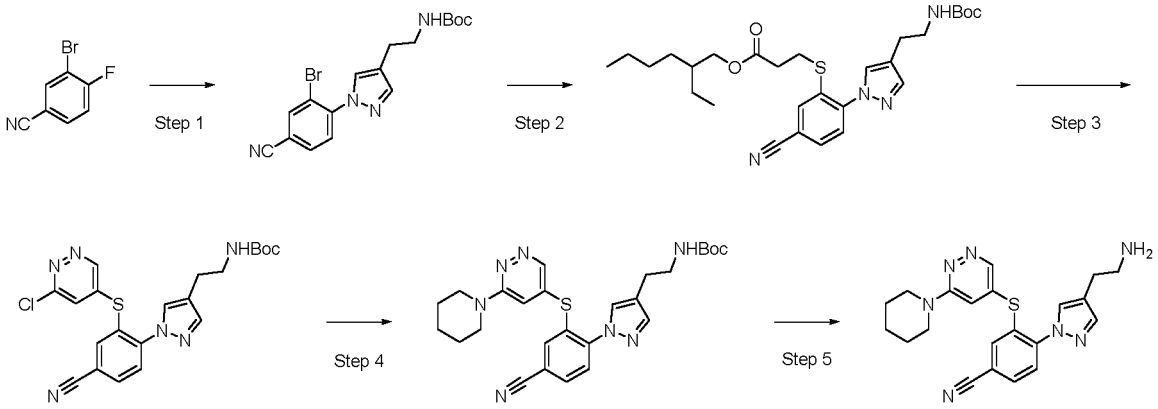
Exact MS: 415.2
Obs. MS $(M+H)^+$: 416.4

[Example 40]

4-[4-(2-Aminoethyl)pyrazol-1-yl]-3-(6-piperidin-1-ylpyridazin-4-yl)sulfanylbenzonitrile (Compound No. 1246)

[0479]

[Chem. 86]



Step 1: tert-Butyl N-[2-[1-(2-bromo-4-cyanophenyl)pyrazol-4-yl]ethyl]carbamate

[0480] DMF (15 mL) was added to 3-bromo-4-fluorobenzonitrile (1.80 g, 9.00 mmol), tert-butyl N-[2-(1H-pyrazol-4-yl)ethyl]carbamate (950 mg, 4.50 mmol) and potassium carbonate (1.87 g, 13.5 mmol), and the mixture was stirred at 150°C for 1 hour. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The solution was dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (1.86 g, containing impurities).
MS: m/z 391.0 $(M+H)^+$.

Step 2: 2-Ethylhexyl 3-[5-cyano-2-[4-[2-[(2-methylpropan-2-yl)oxycarbonylamino]ethyl]pyrazol-1-yl]phenyl]sulfanylpropanoate

[0481] tert-Butyl N-[2-[1-(2-bromo-4-cyanophenyl)pyrazol-4-yl]ethyl]carbamate (500 mg, 1.28 mmol) was dissolved in 1,4-dioxane (5.11 mL), then to the solution, 2-ethylhexyl 3-mercaptopropionate (335 mg, 1.53 mmol), tris(dibenzylideneacetone)dipalladium (58.5 mg, 0.0639 mmol), 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (73.9 mg, 0.128 mmol) and N,N-diisopropylethylamine (0.445 mL, 2.56 mmol) were added, and the mixture was stirred at 100°C for 1 hour. The reaction solution was cooled to room temperature and filtered through Celite, and then the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (723 mg, 96%).
MS: m/z 529.3 $(M+H)^+$.

Step 3: tert-Butyl N-[2-[1-[2-(6-chloropyridazin-4-yl)sulfanyl-4-cyanophenyl]pyrazol-4-yl]ethyl]carbamate

[0482] 2-Ethylhexyl 3-[5-cyano-2-[4-[2-[(2-methylpropan-2-yl)oxycarbonylamino]ethyl]pyrazol-1-yl]phenyl]sulfanylpropanoate (723 mg, 1.37 mmol) was dissolved in DMF (2 mL), then to the solution, 3,5-dichloropyridazine (408 mg, 2.74 mmol) and DBU (0.5 mL) were added, and the mixture was stirred at 50°C for 30 minutes. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The solution was dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (543 mg, 87%).

MS: m/z 401.1 $(M-tBu+H)^+$.
^{1}H-NMR ($CDCl_3$) δ: 8.78 (1H, d, J = 1.8 Hz), 7.95 (1H, d, J = 1.8 Hz), 7.88 (1H, dd, J = 8.5, 2.1 Hz), 7.77 (1H, d, J = 8.2 Hz), 7.72 (1H, s), 7.52 (1H, s), 7.00 (1H, d, J = 1.8 Hz), 4.61 (1H, brs), 3.29 (2H, q, J = 6.6 Hz), 2.66 (2H, t, J = 7.1 Hz), 1.44 (9H, s).

Step 4: tert-Butyl N-[2-[1-[4-cyano-2-(6-piperidin-1-ylpyridazin-4-yl)sulfanylphenyl]pyrazol-4-yl]ethyl]carbamate

[0483] DMF (1 mL) was added to tert-butyl N-[2-[1-[2-(6-chloropyridazin-4-yl)sulfanyl-4-cyanophenyl]pyrazol-4-yl]ethyl]carbamate (60 mg, 0.131 mmol), then to the mixture, piperidine (33.5 mg, 0.394 mmol) and N,N-diisopropylethylamine (0.15 mL) were added, and the mixture was stirred at 100°C for 5 hours. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The solution was dried over anhydrous sodium sulfate, concentrated under reduced pressure, and the crude product was used in the next reaction without further purification.

Step 5: 4-[4-(2-Aminoethyl)pyrazol-1-yl]-3-(6-piperidin-1-ylpyridazin-4-yl)sulfanylbenzonitrile

[0484] Dichloromethane (1 mL) and TFA (0.5 mL) were added to the crude product obtained in Step 4, and the mixture was stirred at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (50.3 mg, 95%).

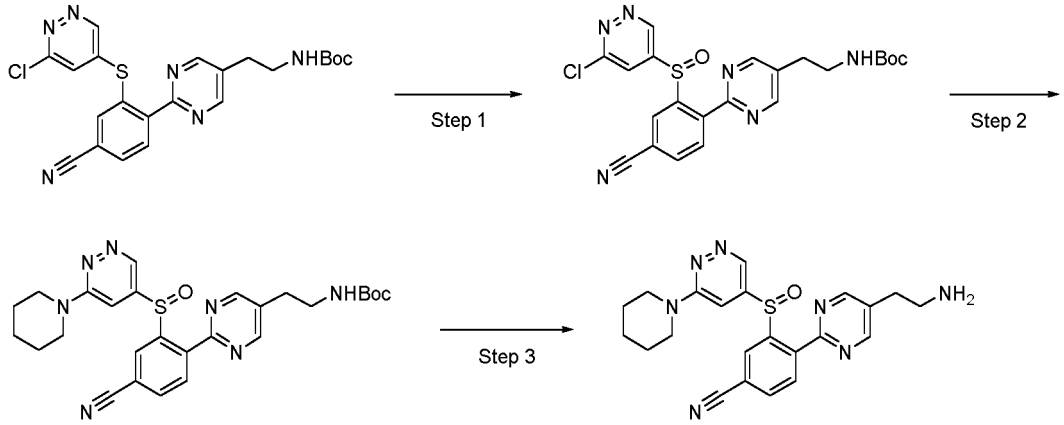
Exact MS: 405.2
Obs. MS $(M+H)^+$: 406.4

[Example 41]

4-[5-(2-Aminoethyl)pyrimidin-2-yl]-3-(6-piperidin-1-ylpyridazin-4-yl)sulfinylbenzonitrile (Compound No. 1276)

[0485]

[Chem. 87]



Step 1: tert-Butyl N-[2-[2-[2-(6-chloropyridazin-4-yl)sulfinyl-4-cyanophenyl]pyrimidin-5-yl]ethyl]carbamate

[0486] Dichloromethane (3.3 mL) was added to tert-butyl N-[2-[2-[2-(6-chloropyridazin-4-yl)sulfanyl-4-cyanophenyl]pyrimidin-5-yl]ethyl]carbamate (154 mg, 0.328 mmol), then to the mixture, 3-chloroperbenzoic acid (75.4 mg, 0.328 mmol) was added at 0°C, and then the reaction mixture was heated to room temperature and stirred for 2 hours. The reaction solution was concentrated under reduced pressure, and the crude product obtained was used in the next reaction. MS: m/z 485.1 $(M+H)^+$.

Step 2:_tert-Butyl_N-[2-[2-[4-cyano-2-(6-piperidin-1-ylpyridazin-4-yl)sulfinylphenyl]pyrimidin-5-yl]ethyl]carbamate

[0487] An aliquot (79.1 mg) of the crude product obtained in Step 1 was dissolved in 1,4-dioxane (1 mL), then to the solution, piperidine (27.8 mg, 0.326 mmol), tris(dibenzylideneacetone)dipalladium (14.9 mg, 0.0163 mmol), 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (18.9 mg, 0.0326 mmol), and cesium carbonate (159 mg, 0.489 mmol) were added, and the mixture was stirred at 100°C for 1 hour. The reaction mixture was cooled to room temperature and filtered through Celite, and then the solution was concentrated under reduced pressure. The crude was used in the next reaction. MS: m/z 534.2 $(M+H)^+$.

Step 3: 4-[5-(2-Aminoethyl)pyrimidin-2-yl]-3-(6-piperidin-1-ylpyridazin-4-yl)sulfinylbenzonitrile

[0488] Dichloromethane (1 mL) and TFA (0.5 mL) were added to the crude product obtained in Step 2, and the mixture was stirred at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (1.72 mg).

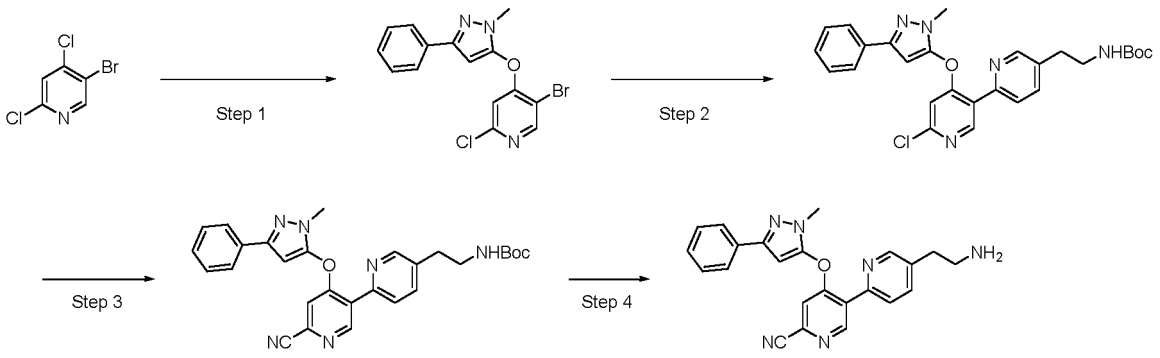
Exact MS: 433.2
Obs. MS $(M+H)^+$: 434.3

[Example 42]

5-[5-(2-Aminoethyl)pyridin-2-yl]-4-(2-methyl-5-phenylpyrazol-3-yl)oxypyridine-2-carbonitrile (Compound No. 1277)

[0489]

[Chem. 88]



Step 1: 5-Bromo-2-chloro-4-(2-methyl-5-phenylpyrazol-3-yl)oxypyridine

[0490] 5-Bromo-2,4-dichloropyridine (230 mg, 1.00 mmol) and 2-methyl-5-phenyl-4H-pyrazol-3-one (170 mg, 1.00 mmol) were dissolved in NMP (4 mL), then to the solution, potassium carbonate (280 mg, 2.00 mmol) was added, and the mixture was stirred at 130°C for 1 hour. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (279 mg, 77%).
MS: m/z 364.0 $(M+H)^+$.

Step 2: tert-Butyl N-[2-[6-[6-chloro-4-(2-methyl-5-phenylpyrazol-3-yl)oxypyridin-3-yl]pyri din-3-yl]ethyl]carbamate

[0491] tert-Butyl N-[2-(6-chloropyridin-3-yl)ethyl]carbamate (77 mg, 0.30 mmol) was dissolved in 1,4-dioxane (1.5 mL), then to the solution, hexamethylditin (128 mg, 0.390 mmol) and tetrakis(triphenylphosphine)palladium (34.7 mg, 0.030 mmol) were added, and the mixture was stirred at 130°C for 1.5 hours. To the reaction mixture, 5-bromo-2-chloro-4-(2-methyl-5-phenylpyrazol-3-yl)oxypyridine (109 mg, 0.300 mmol) and copper(I) iodide (5.7 mg, 0.030 mmol) were added, and the mixture was stirred at 130°C for 2 hours. The reaction solution was cooled to room temperature and filtered through Celite, and then the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (47.2 mg, 31%).
MS: m/z 506.2 $(M+H)^+$.

Step 3: tert-Butyl N-[2-[6-[6-cyano-4-(2-methyl-5-phenylpyrazol-3-yl)oxypyridin-3-yl]pyridin-3-yl]ethyl]carbamate

[0492] tert-Butyl N-[2-[6-[6-chloro-4-(2-methyl-5-phenylpyrazol-3-yl)oxypyridin-3-yl]pyridin-3-yl]ethyl]carbamate (32.2 mg, 0.0636 mmol) was dissolved in DMF (0.13 mL), then to the solution, zinc cyanide (4.5 mg, 0.038 mmol), zinc powder (0.4 mg, 6.4 μmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride-dichloromethane adduct (2.6 mg, 3.2 μmol) were added, and the mixture was stirred at 130°C for 1 hour. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.

Step 4: 5-[5-(2-Aminoethyl)pyridin-2-yl]-4-(2-methyl-5-phenylpyrazol-3-yl)oxypyridine-2-carbonitrile

[0493] Dichloromethane (0.5 mL) and TFA (0.5 mL) were added to the crude product obtained in Step 3, and the mixture was stirred at room temperature for 1 hour. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (3.6 mg).

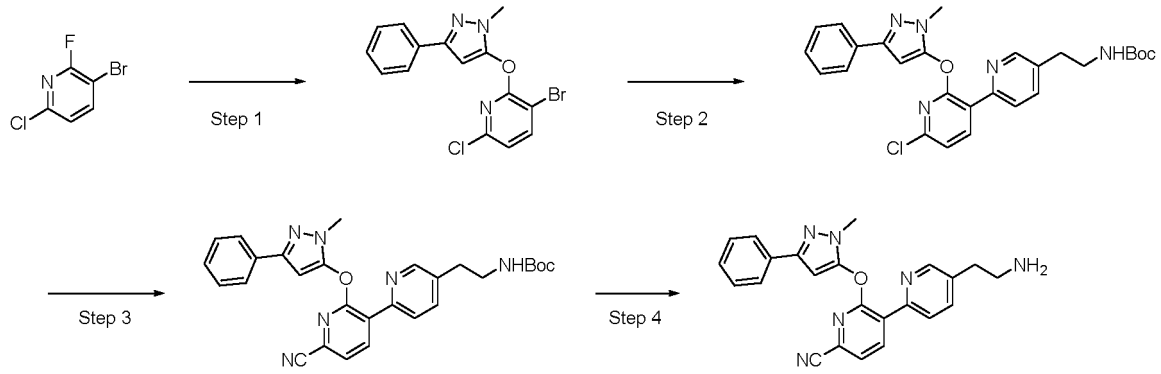
Exact MS: 396.2
Obs. MS $(M+H)^+$: 397.2

[Example 43]

5-[5-(2-Aminoethyl)pyridin-2-yl]-6-(2-methyl-5-phenylpyrazol-3-yl)oxypyridine-2-carbonitrile (Compound No. 1279)

[0494]

[Chem. 89]



Step 1: 3-Bromo-6-chloro-2-(2-methyl-5-phenylpyrazol-3-yl)oxypyridine

[0495] 3-Bromo-6-chloro-2-fluoropyridine (420 mg, 2.00 mmol) and 2-methyl-5-phenyl-4H-pyrazol-3-one (348 mg, 2.00 mmol) were dissolved in NMP (8 mL), then to the solution, potassium carbonate (552 mg, 3.99 mmol) was added, and the mixture was stirred at 130°C for 1 hour. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (495 mg, 68%).
MS: m/z 364.0 $(M+H)^+$.

Step 2: tert-Butyl N-[2-[6-[6-cyano-2-(2-methyl-5-phenylpyrazol-3-yl)oxypyridin-3-yl]pyridin-3-yl]ethyl]carbamate

[0496] tert-Butyl N-[2-(6-chloropyridin-3-yl)ethyl]carbamate (77 mg, 0.30 mmol) was dissolved in 1,4-dioxane (1.5 mL), then to the solution, hexamethylditin (128 mg, 0.390 mmol) and tetrakis(triphenylphosphine)palladium (34.7 mg, 0.030 mmol) were added, and the mixture was stirred at 130°C for 1.5 hours. To the reaction mixture, 3-bromo-6-chloro-2-(2-methyl-5-phenylpyrazol-3-yl)oxypyridine (109 mg, 0.300 mmol) and copper(I) iodide (5.7 mg, 0.030 mmol) were added, and the mixture was stirred at 130°C for 2 hours. The reaction mixture was cooled to room temperature and filtered through Celite, and then the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (32.9 mg, 22%).
MS: m/z 506.2 $(M+H)^+$.

Step 3: tert-Butyl N-[2-[6-[6-cyano-2-(2-methyl-5-phenylpyrazol-3-yl)oxypyridin-3-yl]pyri din-3-yl]ethyl]carbamate

[0497] tert-Butyl N-[2-[6-[6-cyano-2-(2-methyl-5-phenylpyrazol-3-yl)oxypyridin-3-yl]pyridin-3-yl]ethyl]carbamate (20 mg, 0.0395 mmol) was dissolved in DMF (0.13 mL), then to the solution, zinc cyanide (2.8 mg, 0.024 mmol), zinc powder (0.3 mg, 4 μmol), and [1,1'-bis(diphenylphosphino)ferrocene]palladium dichloride-dichloromethane adduct (1.6 mg, 2 μmol) were added, and the mixture was stirred at 130°C for 1 hour. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.
MS: m/z 497.3 $(M+H)^+$.

Step 4: 5-[5-(2-Aminoethyl)pyridin-2-yl]-6-(2-methyl-5-phenylpyrazol-3-yl)oxypyridine-2-carbonitrile

[0498] Dichloromethane (0.5 mL) and TFA (0.5 mL) were added to the crude product obtained in Step 3, and the mixture was stirred at room temperature for 1 hour. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (8.6 mg).

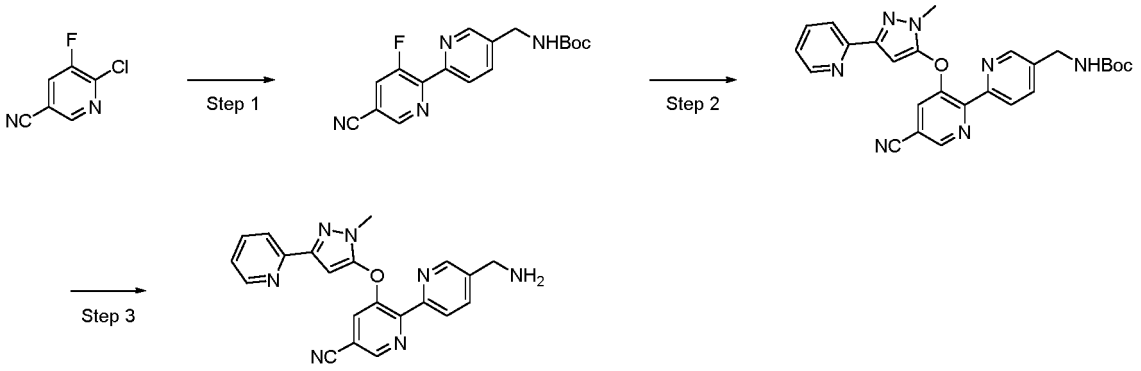
Exact MS: 396.2
Obs. MS $(M+H)^+$: 397.4

[Example 44]

6-[5-(Aminomethyl)pyridin-2-yl]-5-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxypyridine-3-carbonitrile (Compound No. 1289)

[0499]

[Chem. 90]



Step 1: tert-Butyl N-[[6-(5-cyano-3-fluoropyridin-2-yl)pyridin-3-yl]methyl]carbamate

[0500] tert-Butyl N-[(6-chloropyridin-3-yl)methyl]carbamate (72.8 mg, 0.300 mmol) was dissolved in 1,4-dioxane (1.5 mL), then to the solution, hexamethylditin (128 mg, 0.390 mmol) and tetrakis(triphenylphosphine)palladium (34.7 mg, 0.030 mmol) were added, and the mixture was stirred at 130°C for 1.5 hours. To the reaction mixture, 6-chloro-5-fluoropyridine-3-carbonitrile (51.7 mg, 0.330 mmol) and copper(I) iodide (5.7 mg, 0.030 mmol) were added, and the mixture was stirred at 130°C for 2 hours. The reaction mixture was cooled to room temperature and filtered through Celite, and then the solution was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to obtain the target compound (77.9 mg, 79%).
MS: m/z 329.2 $(M+H)^+$.

Step 2: tert-Butyl N-[[6-[5-cyano-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxypyridin-2-yl]pyridin-3-yl]methyl]carbamate

[0501] tert-Butyl N-[[6-(5-cyano-3-fluoropyridin-2-yl)pyridin-3-yl]methyl]carbamate (77.9 mg, 0.237 mmol) and 2-methyl-5-pyridin-2-yl-4H-pyrazol-3-one (41.6 mg, 0.237 mmol) were dissolved in NMP (0.95 mL), then to the solution, potassium carbonate (65.6 mg, 0.475 mmol) was added, and the mixture was stirred at 130°C for 1 hour. The reaction mixture was cooled to room temperature, water was added to the mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate, and the solution was concentrated under reduced pressure. The crude product was used in the next reaction without further purification.

Step 3: 6-[5-(Aminomethyl)pyridin-2-yl]-5-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxypyridine-3-carbonitrile

[0502] Dichloromethane (0.5 mL) and TFA (0.5 mL) were added to the crude product obtained in Step 2, and the mixture was stirred at room temperature for 1 hour. The reaction mixture was concentrated under reduced pressure, and the crude product was purified by HPLC to obtain the target compound (6.9 mg).

Exact MS: 383.2
Obs. MS $(M+H)^+$: 384.2

[Example 45]

[0503] Compounds 1 to 1405 shown in Table 1 above were synthesized by protection, deprotection and the like as necessary according to the synthesis methods described in Examples 1 to 44. The MS data is shown in Table 2 below.

[Table 2-1]

Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$
1	377.2	378.1	41	416.2	417.3	81	400.2	401.1
2	414.2	415.2	42	430.2	431.3	82	408.2	409.3
3	454.2	455.2	43	414.2	415.3	83	418.2	419.3
4	428.2	429.4	44	428.2	429.3	84	435.1	436.2
5	482.2	483.4	45	414.2	415.3	85	416.2	417.3
6	409.2	410.4	46	398.2	399.2	86	407.2	408.3
7	415.2	416.2	47	416.2	417.3	87	351.1	352.2
8	429.2	430.2	48	404.2	405.2	88	351.1	352.0
9	431.2	432.2	49	414.2	415.3	89	402.2	403.3
10	470.2	471.3	50	401.2	402.4	90	400.2	401.3
11	445.2	446.2	51	417.2	418.5	91	402.2	403.3
12	456.2	457.3	52	427.2	428.5	92	400.2	401.1
13	507.2	508.2	53	441.2	442.5	93	417.2	418.3
14	389.2	390.2	54	515.3	516.5	94	435.2	436.3
15	401.2	402.4	55	499.2	500.5	95	427.2	428.3
16	429.3	430.5	56	487.2	488.5	96	450.2	451.3
17	413.2	414.0	57	487.3	488.6	97	476.2	477.2
18	449.2	450.4	58	473.2	474.5	98	471.2	472.2
19	449.2	450.4	59	491.2	492.5	99	468.2	469.3
20	410.2	411.4	60	509.2	510.4	100	459.2	460.2
21	431.2	431.9	61	509.2	510.5	101	483.2	484.2
22	422.2	422.9	62	429.2	430.5	102	393.2	394.3
23	474.2	474.9	63	489.2	490.4	103	393.2	394.3
24	421.2	422.4	64	489.2	490.2	104	440.2	441.3
25	399.2	400.2	65	385.2	386.2	105	449.2	450.3
26	471.2	471.9	66	399.2	400.4	106	459.2	460.3
27	427.2	428.0	67	441.2	442.3	107	400.2	401.3
28	409.2	409.9	68	445.2	446.4	108	402.2	403.3
29	409.2	409.9	69	392.2	393.3	109	414.1	415.2
30	413.1	413.9	70	408.2	409.0	110	411.2	412.3
31	429.2	430.0	71	443.1	444.1	111	464.2	465.2
32	412.1	412.9	72	497.2	498.3	112	424.2	425.3
33	412.1	412.9	73	481.2	482.3	113	469.2	470.2
34	397.2	398.4	74	416.2	417.3	114	393.2	394.3
35	428.1	428.9	75	407.2	408.3	115	394.2	395.3
36	406.2	406.9	76	351.1	352.2	116	410.2	411.2
37	442.2	443.4	77	402.2	403.1	117	476.1	477.2

(continued)

Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$
38	402.2	402.9	78	400.2	401.2	118	422.2	423.2
39	442.2	443.0	79	351.1	352.2	119	449.2	450.2
40	413.1	413.8	80	402.2	403.1	120	450.2	451.2

[Table 2-2]

Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$
121	436.2	437.2	161	411.2	412.3	201	419.2	420.3
122	469.2	470.1	162	396.2	397.3	202	359.2	360.4
123	416.2	417.1	163	395.2	396.3	203	411.2	412.3
124	416.2	417.1	164	409.2	410.3	204	400.2	401.1
125	402.2	403.3	165	412.2	413.3	205	426.2	427.3
126	416.2	417.3	166	408.2	409.3	206	426.2	427.3
127	432.2	433.2	167	425.2	426.2	207	451.2	452.3
128	414.2	415.2	168	438.1	439.2	208	443.2	444.3
129	452.2	453.1	169	421.2	422.3	209	457.2	458.4
130	424.2	425.2	170	412.2	413.2	210	457.2	458.3
131	441.2	442.2	171	412.2	413.2	211	374.2	375.3
132	427.2	428.2	172	415.2	416.3	212	390.2	391.3
133	465.2	466.2	173	415.2	416.2	213	358.2	359.3
134	443.2	444.2	174	395.2	396.3	214	372.2	373.3
135	368.1	369.1	175	395.2	396.3	215	374.2	375.3
136	421.2	422.1	176	396.2	397.3	216	381.1	382.1
137	384.2	385.1	177	411.2	412.2	217	439.2	440.3
138	414.2	415.3	178	396.2	397.3	218	453.2	454.3
139	451.2	452.2	179	396.2	397.2	219	453.2	454.3
140	430.2	431.2	180	425.2	426.3	220	431.1	432.3
141	430.2	431.2	181	410.2	411.3	221	426.2	427.4
142	426.2	427.2	182	410.2	411.3	222	429.1	430.1
143	441.2	442.2	183	428.2	429.2	223	429.1	430.1
144	421.2	422.1	184	413.2	414.3	224	429.1	430.3
145	401.2	402.2	185	413.2	414.2	225	417.1	418.1
146	410.1	411.1	186	412.2	413.3	226	411.2	412.1
147	470.2	471.2	187	413.2	414.3	227	403.2	404.3
148	470.2	471.2	188	408.2	409.3	228	375.2	376.0
149	449.2	450.2	189	422.2	423.3	229	361.2	362.0
150	465.2	466.2	190	425.2	426.2	230	361.2	362.0

(continued)

Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$
151	499.2	500.2	191	448.2	449.1	231	426.2	427.2
152	447.2	448.2	192	438.2	439.2	232	405.2	406.2
153	467.2	468.2	193	438.2	439.2	233	419.2	420.2
154	398.1	399.1	194	415.2	416.3	234	461.3	462.1
155	475.2	476.1	195	429.1	430.2	235	447.2	448.2
156	461.2	462.2	196	387.1	388.3	236	427.2	428.1
157	445.2	446.2	197	430.2	431.3	237	373.2	374.0
158	470.2	471.2	198	428.2	429.3	238	395.1	396.0
159	446.1	447.1	199	413.2	414.3	239	445.2	446.1
160	395.2	396.3	200	412.2	413.1	240	449.2	450.0

[Table 2-3]

Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$
241	420.2	421.2	281	429.2	430.4	321	427.2	428.4
242	376.2	377.1	282	391.2	392.2	322	517.2	518.4
243	416.3	417.1	283	389.2	390.2	323	319.1	320.3
244	468.2	469.0	284	375.2	376.2	324	334.2	335.3
245	417.2	418.2	285	397.2	398.4	325	346.2	347.3
246	415.1	416.1	286	398.2	399.4	326	333.2	334.3
247	443.2	444.1	287	390.2	391.4	327	345.2	346.3
248	412.2	413.0	288	347.2	348.4	328	402.2	403.4
249	412.2	413.1	289	381.2	382.3	329	401.2	402.4
250	416.2	417.4	290	382.2	383.3	330	333.2	334.3
251	449.2	450.3	291	407.2	408.4	331	345.2	346.3
252	441.2	442.0	292	408.2	409.4	332	402.2	403.4
253	487.2	488.0	293	348.2	349.2	333	443.2	444.4
254	399.2	400.1	294	409.2	410.4	334	387.2	388.4
255	391.2	392.2	295	433.2	434.2	335	403.2	404.3
256	455.2	456.3	296	423.2	424.2	336	419.2	420.4
257	455.2	456.3	297	429.2	430.3	337	392.2	393.3
258	407.2	408.2	298	391.2	392.2	338	424.2	425.4
259	405.2	406.3	299	333.2	334.2	339	430.2	431.3
260	362.2	363.3	300	319.1	320.3	340	446.1	447.3
261	362.2	363.3	301	439.2	440.3	341	437.2	438.4
262	400.2	401.1	302	449.2	450.3	342	430.2	431.3
263	429.1	430.3	303	459.2	460.3	343	446.1	447.3

(continued)

Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$
264	387.1	388.4	304	322.2	323.2	344	437.2	438.4
265	420.2	421.3	305	334.2	335.2	345	363.2	364.4
266	434.2	435.2	306	381.1	382.3	346	396.2	397.4
267	408.2	409.3	307	451.2	452.4	347	360.2	361.4
268	434.1	435.3	308	431.2	432.3	348	375.2	376.4
269	406.2	407.3	309	391.2	392.3	349	349.2	350.3
270	420.2	421.3	310	382.2	383.2	350	431.2	432.4
271	442.2	443.3	311	320.1	321.3	351	480.2	481.4
272	374.2	375.3	312	396.2	397.2	352	413.2	414.4
273	404.2	405.3	313	396.2	397.2	353	480.2	481.4
274	396.2	397.3	314	412.2	413.3	354	426.2	427.4
275	408.2	409.3	315	371.2	372.3	355	480.2	481.4
276	389.2	390.4	316	363.1	364.3	356	413.2	414.4
277	394.2	395.3	317	360.2	361.3	357	480.2	481.4
278	390.2	391.4	318	391.2	392.4	358	426.2	427.4
279	451.2	452.4	319	376.2	377.4	359	378.2	379.3
280	428.2	429.2	320	441.2	442.4	360	414.2	415.3

[Table 2-4]

Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$
361	347.2	384.4	401	359.2	360.3	441	390.2	391.2
362	347.2	348.4	402	414.2	415.3	442	419.2	420.3
363	348.2	349.3	403	429.2	430.3	443	345.2	346.2
364	348.2	349.3	404	430.2	431.3	444	466.2	467.3
365	411.2	412.3	405	391.2	392.4	445	442.2	443.3
366	411.2	412.4	406	392.2	393.4	446	457.2	458.3
367	376.2	377.4	407	403.2	404.4	447	415.2	416.3
368	417.2	418.3	408	404.2	405.4	448	401.2	402.3
369	402.2	403.4	409	459.2	460.3	449	489.2	490.3
370	443.2	444.3	410	445.2	446.3	450	331.1	332.2
371	408.2	409.2	411	444.2	445.3	451	331.1	332.2
372	376.2	377.3	412	431.2	432.3	452	381.2	382.2
373	376.2	377.3	413	391.2	392.4	453	381.2	382.2
374	375.2	376.3	414	371.1	372.3	454	442.2	443.3
375	375.2	376.3	415	407.1	408.3	455	429.2	430.3
376	438.1	439.2	416	331.1	332.2	456	428.2	429.3

(continued)

Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$
377	445.1	446.2	417	332.1	333.2	457	421.2	422.2
378	425.2	426.4	418	444.2	445.3	458	418.2	419.3
379	428.2	429.3	419	486.2	487.4	459	417.2	418.3
380	388.2	389.3	420	376.2	377.3	460	429.2	430.3
381	424.2	425.4	421	375.2	376.3	461	388.2	389.3
382	403.2	404.4	422	370.2	371.2	462	428.2	429.3
383	439.2	440.4	423	426.2	427.3	463	372.2	373.3
384	370.1	371.3	424	415.2	416.3	464	442.2	443.2
385	376.2	377.3	425	471.2	472.4	465	443.2	444.3
386	364.2	365.3	426	389.1	390.3	466	423.2	424.3
387	432.2	433.3	427	401.2	402.3	467	403.2	404.2
388	416.2	417.4	428	425.1	426.3	468	371.1	372.2
389	404.2	405.4	429	431.2	432.3	469	411.2	412.2
390	402.1	403.2	430	432.2	433.3	470	430.2	431.3
391	403.1	404.3	431	375.2	376.3	471	430.2	431.3
392	403.2	404.3	432	375.2	376.3	472	395.1	396.2
393	388.2	389.4	433	423.1	424.2	473	417.2	418.2
394	383.1	384.3	434	417.2	418.2	474	413.1	414.2
395	410.2	411.3	435	458.2	459.3	475	371.1	372.2
396	396.2	397.2	436	402.2	403.2	476	444.2	445.3
397	429.2	430.4	437	360.2	361.2	477	388.2	389.3
398	415.2	416.4	438	345.2	346.2	478	446.2	447.3
399	379.2	380.2	439	466.2	467.3	479	448.2	449.3
400	373.2	374.3	440	389.2	390.3	480	345.2	346.2

[Table 2-5]

Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$
481	359.2	360.2	521	388.1	389.1	561	461.2	462.2
482	359.2	360.2	522	421.2	422.2	562	457.2	458.2
483	390.2	391.2	523	460.2	461.2	563	444.2	445.2
484	389.2	390.2	524	461.2	462.2	564	443.2	444.2
485	404.2	405.3	525	423.2	424.2	565	470.2	471.3
486	456.2	457.3	526	424.2	425.2	566	431.2	432.3
487	458.2	459.3	527	443.2	444.2	567	431.2	432.2
488	444.2	445.3	528	444.2	445.2	568	470.2	471.2
489	416.2	417.2	529	445.2	446.2	569	470.2	471.2

(continued)

Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$
490	430.2	431.3	530	446.2	447.2	570	399.2	400.2
491	402.2	403.2	531	459.2	460.2	571	411.2	412.3
492	405.2	406.2	532	460.2	461.2	572	394.2	395.2
493	384.2	385.3	533	429.2	430.2	573	375.2	376.2
494	440.2	441.2	534	389.2	390.2	574	419.1	420.1
495	390.2	391.2	535	389.2	390.2	575	376.2	377.2
496	389.2	390.2	536	418.1	419.1	576	350.1	351.2
497	481.3	482.2	537	443.2	444.2	577	334.2	335.2
498	415.2	416.2	538	445.2	446.2	578	428.2	429.2
499	416.2	417.2	539	471.2	472.2	579	408.2	409.2
500	429.2	430.2	540	413.2	414.2	580	430.2	431.2
501	430.2	431.2	541	402.2	403.2	581	443.2	444.2
502	419.2	420.2	542	388.2	389.2	582	352.1	353.1
503	404.2	405.2	543	362.2	363.2	583	388.1	389.1
504	388.2	389.2	544	418.2	419.2	584	335.1	336.1
505	459.2	460.2	545	404.2	405.2	585	389.2	390.2
506	460.2	416.2	546	378.2	379.2	586	389.2	390.2
507	416.2	417.2	547	376.2	377.2	587	396.2	397.2
508	417.2	418.2	548	392.2	393.2	588	402.1	403.2
509	430.2	431.2	549	392.2	393.2	589	422.2	423.2
510	431.2	432.2	550	445.2	446.2	590	441.2	442.2
511	413.2	414.2	551	402.2	403.2	591	418.2	419.2
512	397.2	398.2	552	428.2	429.2	592	389.1	390.1
513	453.2	454.2	553	442.2	443.2	593	408.1	409.1
514	419.2	420.2	554	442.2	443.2	594	371.1	372.2
515	385.2	386.2	555	442.2	443.2	595	414.1	415.1
516	424.2	425.2	556	375.2	376.2	596	398.1	399.2
517	431.2	432.2	557	404.2	405.2	597	409.2	410.2
518	409.1	352.1	558	446.2	447.2	598	415.1	416.1
519	375.2	376.2	559	447.2	448.2	599	409.2	410.2
520	351.1	352.1	560	460.2	461.2	600	444.1	445.1

[Table 2-6]

Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$
601	444.1	445.1	641	385.2	386.1	681	402.2	403.2
602	429.1	430.1	642	382.2	383.1	682	383.1	384.2

(continued)

Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$
603	430.1	431.1	643	360.2	361.2	683	359.2	360.3
604	424.2	425.2	644	374.2	375.2	684	360.2	361.3
605	443.1	444.1	645	371.2	372.2	685	360.2	361.3
606	444.1	445.1	646	372.2	373.2	686	409.2	410.3
607	407.1	408.2	647	415.2	416.2	687	411.2	412.3
608	388.1	389.2	648	416.2	417.2	688	424.2	425.3
609	382.2	383.2	649	401.1	402.2	689	429.1	430.2
610	401.2	402.2	650	397.2	398.2	690	413.1	414.3
611	459.2	460.2	651	401.1	402.2	691	423.2	424.3
612	403.2	404.2	652	397.2	398.1	692	424.2	425.3
613	457.2	458.2	653	409.1	410.3	693	424.2	425.3
614	459.2	460.2	654	493.2	494.3	694	443.1	444.3
615	403.2	404.2	655	377.2	378.2	695	343.1	344.2
616	442.2	443.2	656	391.2	392.2	696	372.2	373.3
617	422.2	423.1	657	386.2	387.2	697	386.2	387.3
618	389.1	390.2	658	387.2	388.2	698	346.2	347.3
619	401.2	402.2	659	360.2	361.2	699	387.1	388.1
620	403.2	404.2	660	361.2	362.2	700	388.0	389.1
621	388.2	389.2	661	458.2	459.2	701	416.2	417.3
622	374.2	375.2	662	423.2	424.2	702	397.2	398.3
623	348.2	349.2	663	425.2	426.2	703	401.1	402.3
624	389.2	390.2	664	439.2	440.2	704	407.2	408.3
625	375.2	376.2	665	453.2	454.2	705	386.1	387.2
626	349.2	350.1	666	517.3	518.3	706	400.1	401.2
627	403.2	404.2	667	474.2	475.2	707	393.1	394.2
628	389.2	390.2	668	433.2	434.2	708	417.2	418.3
629	363.2	364.2	669	419.2	420.2	709	431.2	432.3
630	375.2	376.1	670	468.2	469.2	710	431.2	432.3
631	361.2	362.1	671	427.2	428.2	711	386.2	387.3
632	375.2	376.1	672	413.2	414.2	712	391.1	392.2
633	373.2	374.1	673	467.2	468.2	713	344.1	345.2
634	389.2	390.2	674	426.2	427.2	714	373.2	374.2
635	417.2	418.1	675	412.2	413.2	715	387.2	388.2
636	431.2	432.1	676	307.1	308.1	716	347.1	348.2
637	389.2	390.2	677	321.1	322.1	717	408.1	409.2
638	415.2	416.2	678	346.2	347.1	718	363.1	364.1
639	391.2	392.1	679	362.1	363.1	719	392.1	393.2

(continued)

Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$
640	415.1	416.2	680	346.2	347.1	720	365.1	366.1

[Table 2-7]

Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$
721	383.1	384.1	761	443.1	444.2	801	376.2	377.3
722	397.1	398.2	762	452.2	453.3	802	362.2	363.2
723	409.1	410.2	763	361.2	362.2	803	362.2	363.1
724	395.2	396.2	764	361.2	362.3	804	376.2	377.3
725	379.1	380.2	765	375.2	376.3	805	362.2	363.2
726	393.1	394.2	766	375.1	376.3	806	362.2	363.2
727	367.1	368.1	767	419.2	420.2	807	422.1	423.3
728	364.1	365.1	768	425.2	426.3	808	397.2	398.3
729	401.1	402.1	769	403.2	404.3	809	397.2	398.3
730	401.1	402.1	770	391.2	392.3	810	373.1	374.3
731	385.2	386.2	771	405.2	406.3	811	374.1	375.3
732	422.2	423.2	772	391.2	392.3	812	388.1	389.3
733	441.2	442.2	773	390.2	391.3	813	363.2	364.3
734	411.2	412.2	774	377.2	378.3	814	349.2	350.2
735	430.2	431.2	775	391.2	392.3	815	421.1	422.3
736	384.2	385.2	776	360.2	361.3	816	421.1	422.3
737	421.2	422.2	777	360.2	361.2	817	381.1	382.3
738	452.2	453.3	778	428.2	429.3	818	388.2	389.3
739	411.2	412.2	779	414.2	415.3	819	376.2	377.3
740	397.2	398.2	780	428.2	429.3	820	397.1	398.2
741	430.2	431.3	781	442.2	443.3	821	401.2	402.4
742	444.2	445.3	782	456.2	457.3	822	395.2	396.4
743	404.2	405.3	783	442.2	443.3	823	427.2	428.3
744	415.2	416.2	784	404.2	405.3	824	387.2	388.4
745	415.2	416.3	785	472.2	473.3	825	403.2	404.4
746	415.2	416.3	786	413.2	414.3	826	412.2	413.4
747	415.2	416.3	787	431.2	432.3	827	426.2	427.3
748	437.2	438.3	788	388.2	389.3	828	355.1	356.3
749	423.2	424.2	789	373.2	374.3	829	356.1	357.3
750	386.2	387.2	790	375.2	376.4	830	397.2	398.2
751	372.2	373.3	791	389.2	390.4	831	383.1	384.2
752	412.2	413.3	792	389.2	390.4	832	397.2	398.2

(continued)

Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$
753	398.2	399.2	793	391.2	392.1	833	383.1	384.2
754	390.2	391.3	794	401.2	402.4	834	402.1	403.2
755	402.2	403.2	795	401.2	402.4	835	388.1	389.2
756	481.2	482.3	796	401.2	402.4	836	402.1	403.2
757	481.2	482.3	797	405.2	406.4	837	388.1	389.2
758	405.2	406.3	798	393.2	394.3	838	435.2	436.5
759	419.2	420.3	799	392.2	393.2	839	509.3	510.4
760	407.2	408.2	800	421.2	422.3	840	528.3	529.4

[Table 2-8]

Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$
841	451.2	452.2	881	414.2	415.4	921	416.2	417.3
842	405.2	406.4	882	387.1	388.3	922	402.2	403.3
843	392.2	393.4	883	438.2	439.3	923	373.2	374.2
844	404.2	405.4	884	430.1	431.4	924	384.2	385.4
845	404.2	405.4	885	432.2	433.2	925	384.2	385.4
846	390.2	391.4	886	404.2	405.3	926	386.1	387.0
847	424.1	425.4	887	402.2	403.4	927	370.1	371.3
848	390.2	391.4	888	418.2	419.4	928	401.1	402.2
849	404.2	405.4	889	418.2	419.3	929	384.0	385.1
850	400.2	401.4	890	406.2	407.4	930	384.1	385.2
851	401.2	402.4	891	412.1	413.3	931	384.1	385.2
852	403.2	404.4	892	388.2	389.3	932	384.1	385.2
853	387.2	388.4	893	416.1	417.3	933	400.2	401.2
854	389.2	390.4	894	418.2	419.4	934	384.1	385.2
855	401.2	402.4	895	390.1	391.3	935	389.1	390.2
856	403.2	404.4	896	376.2	377.3	936	386.2	387.2
857	403.2	404.4	897	398.1	399.3	937	390.2	391.2
858	405.2	406.4	898	374.1	375.3	938	390.2	391.2
859	415.2	416.4	899	416.2	417.3	939	390.2	391.2
860	415.2	416.4	900	430.2	431.3	940	398.2	399.2
861	415.2	416.4	901	402.2	403.4	941	411.2	412.2
862	419.2	420.4	902	416.2	417.4	942	376.2	377.2
863	435.2	436.4	903	406.1	407.3	943	416.2	417.2
864	402.2	403.4	904	406.1	407.3	944	417.2	418.3
865	388.2	389.4	905	381.2	382.4	945	386.2	387.2

(continued)

Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$
866	447.1	448.3	906	381.2	382.3	946	386.2	387.2
867	421.2	422.4	907	362.2	363.3	947	386.2	387.2
868	435.2	436.3	908	348.2	349.3	948	389.1	390.0
869	432.2	433.4	909	380.2	381.2	949	398.2	399.0
870	346.2	347.3	910	380.2	381.2	950	398.2	399.2
871	402.2	403.3	911	388.1	389.2	951	403.1	404.0
872	434.2	435.3	912	383.1	384.2	952	403.1	404.0
873	399.2	400.2	913	409.2	410.4	953	390.2	391.1
874	413.2	414.3	914	409.2	410.4	954	390.2	391.2
875	427.2	428.3	915	408.2	409.4	955	430.2	431.1
876	434.2	435.4	916	408.2	409.4	956	377.2	378.2
877	461.2	462.3	917	402.2	403.3	957	403.1	404.2
878	435.2	436.4	918	388.2	389.3	958	403.1	404.1
879	417.2	418.4	919	416.2	417.3	959	403.1	404.1
880	415.2	416.2	920	402.2	403.3	960	403.1	404.1

[Table 2-9]

Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$
961	404.1	405.2	1001	409.2	410.0	1041	402.2	403.3
962	403.1	404.2	1002	396.2	397.0	1042	428.2	429.3
963	403.1	404.1	1003	395.2	396.0	1043	375.2	376.1
964	344.1	345.2	1004	376.1	377.0	1044	360.2	361.2
965	410.2	411.4	1005	363.1	364.0	1045	346.2	347.2
966	369.2	370.4	1006	395.2	396.0	1046	372.2	373.2
967	369.2	370.3	1007	383.2	384.2	1047	358.2	359.2
968	395.1	396.5	1008	382.2	383.2	1048	401.1	402.1
969	390.2	391.2	1009	397.2	398.2	1049	414.2	415.2
970	395.1	396.5	1010	396.2	397.1	1050	387.1	388.1
971	390.2	391.5	1011	340.2	342.1	1051	361.2	362.2
972	384.2	385.2	1012	341.2	341.1	1052	396.1	397.0
973	398.2	399.2	1013	355.2	356.2	1053	415.2	416.3
974	384.2	385.2	1014	354.2	355.2	1054	360.2	361.2
975	397.2	398.3	1015	339.1	340.1	1055	382.1	383.0
976	383.2	384.2	1016	338.2	339.1	1056	388.2	389.2
977	390.2	391.4	1017	353.2	354.1	1057	372.2	373.1
978	409.2	410.2	1018	352.2	353.1	1058	358.2	359.1

(continued)

Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$
979	382.2	383.2	1019	381.1	382.1	1059	432.2	433.2
980	381.2	382.2	1020	357.1	358.2	1060	374.2	375.2
981	341.2	342.2	1021	371.2	372.2	1061	389.2	390.1
982	355.2	356.2	1022	379.1	380.1	1062	415.2	416.2
983	355.2	356.2	1023	397.1	398.2	1063	401.2	402.1
984	355.2	356.2	1024	392.1	393.2	1064	420.1	421.2
985	383.2	384.2	1025	360.2	361.3	1065	434.2	435.2
986	383.2	384.2	1026	346.2	347.3	1066	419.1	420.1
987	406.2	407.2	1027	417.2	418.4	1067	419.1	420.2
988	405.2	406.2	1028	403.2	404.3	1068	433.2	434.2
989	420.2	421.2	1029	402.2	403.3	1069	420.1	421.1
990	419.2	420.3	1030	374.2	375.4	1070	434.2	435.1
991	383.2	384.2	1031	388.2	389.4	1071	401.2	402.2
992	370.2	371.2	1032	403.2	404.4	1072	387.2	388.2
993	392.2	393.2	1033	386.2	387.5	1073	439.2	440.1
994	406.2	407.2	1034	386.2	387.5	1074	425.2	426.1
995	368.2	369.2	1035	372.2	373.4	1075	360.2	361.1
996	367.2	368.2	1036	372.2	373.4	1076	433.2	434.1
997	342.2	343.0	1037	395.1	396.3	1077	487.1	488.1
998	341.2	342.0	1038	381.1	382.2	1078	488.1	489.1
999	356.2	357.0	1039	403.1	404.1	1079	413.2	414.1
1000	355.2	356.0	1040	429.2	430.2	1080	473.1	474.0

[Table 2-10]

Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$
1081	402.2	403.1	1121	344.2	345.3	1161	427.2	428.2
1082	390.1	391.1	1122	369.2	370.3	1162	428.2	429.2
1083	403.2	404.1	1123	370.2	371.3	1163	387.2	388.2
1084	404.2	405.1	1124	446.2	447.2	1164	388.2	389.2
1085	389.1	390.1	1125	460.2	461.3	1165	417.2	418.3
1086	403.2	404.1	1126	388.2	389.2	1166	418.2	419.2
1087	474.1	475.1	1127	384.2	384.9	1167	381.2	382.3
1088	419.1	420.1	1128	398.2	399.1	1168	367.2	368.2
1089	390.1	391.1	1129	394.2	395.2	1169	381.2	382.3
1090	391.1	392.1	1130	408.2	409.2	1170	367.2	368.2
1091	404.2	407.1	1131	379.2	380.3	1171	360.2	361.3

(continued)

Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$
1092	405.2	406.1	1132	379.2	380.3	1172	346.2	347.3
1093	406.1	408.1	1133	395.2	396.4	1173	386.1	387.2
1094	420.1	421.1	1134	380.2	381.3	1174	372.1	373.2
1095	407.1	408.1	1135	380.2	381.2	1175	401.2	402.3
1096	421.1	422.1	1136	395.2	396.4	1176	368.2	369.2
1097	421.2	422.3	1137	394.2	395.4	1177	433.2	434.3
1098	375.1	376.2	1138	395.2	396.4	1178	375.2	376.4
1099	361.1	362.2	1139	409.2	410.3	1179	415.2	416.4
1100	325.1	326.1	1140	375.2	376.4	1180	483.2	484.4
1101	365.2	366.2	1141	376.2	377.4	1181	389.2	390.4
1102	353.2	354.2	1142	390.2	391.4	1182	380.2	381.3
1103	422.2	423.0	1143	397.2	398.4	1183	366.2	367.2
1104	408.2	409.2	1144	413.1	414.3	1184	361.2	362.3
1105	396.2	397.0	1145	393.2	394.4	1185	347.2	348.3
1106	409.2	410.0	1146	393.2	394.4	1186	387.2	388.3
1107	410.2	411.0	1147	397.2	398.4	1187	345.2	346.2
1108	365.2	366.2	1148	393.2	394.4	1188	347.2	348.3
1109	351.1	352.1	1149	397.2	398.4	1189	333.2	334.2
1110	364.2	365.2	1150	393.2	394.4	1190	373.2	374.3
1111	378.2	379.3	1151	407.2	408.4	1191	331.2	332.2
1112	378.2	379.3	1152	411.2	412.4	1192	399.2	400.2
1113	387.2	388.3	1153	407.2	408.4	1193	412.2	413.2
1114	401.2	402.3	1154	411.2	412.4	1194	413.2	414.3
1115	401.2	402.2	1155	407.2	408.4	1195	360.2	361.0
1116	346.2	347.1	1156	411.2	412.4	1196	346.2	347.0
1117	388.2	389.2	1157	394.2	395.3	1197	381.2	382.2
1118	346.2	347.3	1158	393.2	394.3	1198	373.2	374.2
1119	388.2	389.3	1159	373.2	374.3	1199	374.2	375.2
1120	392.2	393.2	1160	380.2	381.3	1200	389.2	390.2

[Table 2-11]

Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$
1201	380.2	381.1	1241	401.2	402.4	1281	361.2	362.2
1202	395.2	396.2	1242	418.2	419.4	1282	400.2	401.5
1203	394.2	395.2	1243	416.2	417.4	1283	384.1	385.4
1204	414.2	415.3	1244	402.2	403.4	1284	416.2	417.4

(continued)

Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$	Compound number	Exact MS	Obs MS $(M+H)^+$
1205	381.2	382.1	1245	407.2	408.3	1285	403.2	404.2
1206	375.2	376.2	1246	405.2	406.4	1286	395.1	396.2
1207	389.2	390.2	1247	391.2	392.4	1287	384.1	385.2
1208	388.2	389.2	1248	432.2	433.2	1288	382.2	383.3
1209	347.2	348.1	1249	430.2	431.3	1289	383.1	384.2
1210	373.2	374.2	1250	416.2	417.4	1290	405.1	406.3
1211	387.2	388.2	1251	421.2	422.4	1291	391.1	392.2
1212	386.2	387.2	1252	419.2	420.3	1292	405.1	406.2
1213	387.2	388.2	1253	405.2	406.4	1293	391.1	392.3
1214	395.2	396.3	1254	433.2	434.3			
1215	394.2	395.3	1255	431.2	432.4			
1216	361.2	363.3	1256	417.2	418.4			
1217	360.2	361.2	1257	419.2	420.3			
1218	401.2	402.4	1258	417.2	418.3			
1219	400.2	401.4	1259	403.2	404.3			
1220	374.2	375.0	1260	432.2	433.2			
1221	352.2	353.0	1261	418.2	419.2			
1222	353.2	354.1	1262	403.2	404.2			
1223	339.2	340.0	1263	377.1	378.3			
1224	367.2	368.3	1264	388.1	389.2			
1225	353.2	354.3	1265	389.1	390.2			
1226	427.2	428.5	1266	362.1	363.2			
1227	439.2	440.5	1267	363.1	364.2			
1228	425.2	426.2	1268	403.2	404.2			
1229	395.2	396.3	1269	409.1	410.1			
1230	425.2	426.3	1270	423.1	424.2			
1231	409.2	410.3	1271	411.1	412.2			
1232	416.1	417.2	1272	377.1	378.2			
1233	375.2	376.4	1273	391.2	392.3			
1234	376.2	377.2	1274	440.1	441.3			
1235	390.2	391.1	1275	426.1	427.2			
1236	404.2	405.2	1276	433.2	434.3			
1237	429.2	430.2	1277	396.2	397.2			
1238	433.2	434.1	1278	382.2	383.2			
1239	417.2	418.4	1279	396.2	397.4			
1240	415.2	416.4	1280	397.2	398.3			

[Example 46]

Evaluation of TRPC6 channel inhibitory activity (1) (Compound Nos. 1-1293)

[0504] In order to investigate TRPC6 channel inhibitory activity of the compounds, evaluation was conducted using FLIPR(R) Calcium 5 Assay Kit (Molecular Devices) in accordance with the following procedure. Human TRPC6 stably-expressing cells were seeded in a 384-well black clear bottom plate at a density of 5×10^3/well and cultured in an incubator at 37°C 5% CO_2 for 24 hours. Thereafter, 25 μL of a Non Wash Dye Solution, prepared using Component A, 20 mM HEPES-HBSS and 250 mM probenecid, all of which are included in the kit, was added to each well, and the plate was incubated for 30 minutes. A volume of 12.5 μL of a compound solution was added into each well while the fluorescence was measured with FLIPR tetra. After 20 minutes, 12.5 μL of a 1-oleoyl-2-acetyl glycerol (OAG) solution was added at a final concentration of 30 μM. The difference between the minimum fluorescence intensity before the addition of the compound and the maximum fluorescence intensity after the addition of OAG was defined as a signal. An inhibition rate was calculated, assuming the average signal of wells without the compound as the inhibition rate of 0% and the average signal of wells without the compound and OAG as the inhibition rate of 100%. The calculated inhibition rate was analyzed by a four-parameter logistic regression to quantify the inhibition rate in the logarithm of the inverse of the effective concentration which gives a 50% inhibition rate (pIC_{50}). The results are shown in the following Table 3. The intensity was expressed by the following symbols (+, ++, +++).

+: pIC_{50} <6.0
++: $6.0 \leq pIC_{50}$ <8.0
+++: $8.0 \leq pIC_{50}$

[Example 47]

Evaluation of TRPC6 channel inhibitory activity (2) (Compound Nos. 1293 to 1405)

[0505] The activity of the TRPC6 inhibitor was measured by stimulating HEK293 cells, in which human TRPC6 was stably introduced, with OAG (1-Oleoyl-2-acetyl-sn-glycerol, Miliipore Sigma, 06754), using the FLIPR tetra system. The cells were proliferated in a humid environment at 37°C 5% CO_2 using a growth medium (DMEM (Dulbecco's Modified Eagle's Medium) high glucose containing 10% fetal bovine serum, 1 × PSGlu (penicillin-streptomycin glutamine), 1 × NEAA (Non-essential amino acid), sodium pyruvate and 200 μg/mL hyglomycin. For cell subculture, the cells were proliferated to 70-90% confluence, and gently washed twice with PBS (phosphate-buffered saline) free of calcium and magnesium after removing the medium. Then, the cells were incubated at 37°C for 5 minutes after adding trypsin (3 mL), peeled off by tapping the flask at the base of the hand, 7 mL of growth medium was added to inactivate trypsin, and then the cells were resuspended. Usually, the cells were separated every 2-3 days to become a cell density of 1/5. The day before evaluation, the cells were seeded in a poly-D-lysine (PDL) coated 384-well plate using a multi-channel pipette or multidrop at a cell density of 1.0-1.5 × 10^4 cells/25 μL/well. After culturing overnight in a PDL-coated 384 Blackwell plate, a fluorescent dye buffer was added first to the cells and the cells were cultured at room temperature for 90-120 minutes. For preparing 10 mL of fluorescent dye buffer, 9 mL of assay buffer, 1 mL of 10 × PBX signal enhancer, and 10 μL of calcium indicator were mixed. Cells treated with the compounds of each level 25 minutes before the stimulation with OAG of TRPC6 agonist were incubated. OAG solution was prepared by adding OAG to assay buffer (Ca ringer solution base: 10 mM HEPES (4- (2-hydroxyetkyl)-1-piperazine-ethanesulfonic acid), 4 mM $MgCl_2$, 120 mM NaCl, 5 mM KCl, pH = 7.2 (25°C) + 0.1% BSA + 2 mM $CaCl_2$) to give an OAG concentration of 0.2 mM/2% DMSO. The final concentration of OAG added to the cells is 50 μM/0.5% DMSO. A volume of 12.5 μL of OAG solution was added, and activation of TRPC6 channel was measured using the FLIPR tetra system assaying the change in intracellular calcium level as an index. The 180 seconds imaging frame was defined as the background signal, and the subtraction of the background signal from the raw data was used as the fluorescence peak signal. Each fluorescence peak signal is standardized using an OAG-induced signal and buffer-induced signal as 100% and 0%, respectively. The inhibition rate obtained by plotting the peak signal after the addition of the compounds of each level was analyzed by a four-parameter logistic regression to quantify the inhibition rate in the logarithm of the inverse of the effective concentration which gives a 50% inhibition rate (pIC_{50}). The results are shown in the following Table 3. The intensity was expressed by the above-mentioned symbols (+, ++, +++).

[0506]

[Table 3-1]

Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity
1	++	41	+	81	+	121	+	161	+++
2	+++	42	+	82	+++	122	++	162	+++
3	++	43	++	83	+	123	++	163	++
4	+	44	+	84	++	124	++	164	+++
5	+	45	++	85	++	125	++	165	++
6	+++	46	+++	86	++	126	+	166	++
7	+++	47	++	87	+	127	+	167	++
8	+	48	++	88	+	128	+	168	++
9	+++	49	++	89	+	129	+	169	+
10	+	50	+++	90	++	130	+++	170	+++
11	+++	51	+	91	+	131	+	171	+++
12	+	52	++	92	+	132	++	172	+++
13	++	53	++	93	+++	133	+++	173	+++
14	+	54	+	94	+	134	++	174	+++
15	++	55	+	95	+	135	+	175	+++
16	++	56	+	96	+	136	++	176	+++
17	+++	57	+	97	+	137	+++	177	+++
18	++	58	++	98	+	138	+++	178	++
19	++	59	++	99	+	139	++	179	+++
20	++	60	++	100	+++	140	++	180	+++
21	+++	61	+	101	+++	141	++	181	++
22	++	62	+++	102	++	142	++	182	+++
23	++	63	+	103	++	143	+	183	+++

(continued)

Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity
24	++	64	+	104	+	144	++	184	++
25	+++	65	+++	105	+	145	++	185	+++
26	+++	66	+++	106	+	146	+	186	+++
27	++	67	++	107	++	147	++	187	+++
28	++	68	++	108	++	148	++	188	+
29	++	69	+++	109	+	149	+++	189	+
30	+++	70	+++	110	+	150	+++	190	+++
31	++	71	++	111	++	151	++	191	+
32	+++	72	++	112	+++	152	++	192	++
33	+++	73	++	113	+++	153	+++	193	+
34	++	74	++	114	++	154	++	194	+
35	++	75	++	115	+++	155	++	195	++
36	++	76	+	116	++	156	++	196	++
37	+	77	+	117	++	157	+++	197	+++
38	+	78	++	118	++	158	++	198	++
39	+	79	+	119	+	159	+++	199	+++
40	+	80	+	120	+++	160	+++	200	+

[Table 3-2]

Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity
201	+	241	+++	281	+	321	+++	361	+++
202	+++	242	+	282	++	322	++	362	+++
203	++	243	+	283	++	323	++	363	+++
204	+++	244	++	284	++	324	+++	364	+++
205	+++	245	++	285	+++	325	+++	365	+++
206	+++	246	+++	286	++	326	+++	366	+++
207	++	247	+++	287	+++	327	+++	367	+++
208	+	248	+++	288	+++	328	+++	368	++
209	+	249	+++	289	+++	329	+++	369	++
210	+	250	+++	290	++	330	+	370	+++
211	+++	251	+	291	+	331	++	371	+++
212	+++	252	+	292	++	332	+++	372	+++
213	+++	253	+++	293	+++	333	+++	373	+++
214	++	254	+++	294	+++	334	+++	374	+++
215	+++	255	++	295	+++	335	+++	375	+++
216	++	256	++	296	+++	336	+++	376	+++
217	+	257	++	297	++	337	+++	377	++
218	+	258	+++	298	++	338	+++	378	+++
219	++	259	++	299	+++	339	++	379	+++
220	+	260	+++	300	++	340	++	380	++
221	++	261	+++	301	+++	341	+++	381	+++
222	++	262	+++	302	++	342	++	382	+++
223	++	263	++	303	++	343	++	383	+++
224	++	264	+++	304	+	344	+++	384	+++
225	+++	265	++	305	++	345	++	385	++

(continued)

Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity
226	+++	266	+++	306	+++	346	+++	386	++
227	+++	267	+++	307	++	347	+	387	++
228	+++	268	++	308	++	348	+++	388	+++
229	+++	369	++	309	++	349	+	389	++
230	+++	270	++	310	+++	350	++	391	+++
231	+++	271	++	311	+	351	++	391	+++
232	+++	272	+++	312	+++	352	++	392	+++
233	+++	273	+++	313	+++	353	++	393	+++
234	+	274	+++	314	+++	354	++	394	+++
235	++	275	+++	315	+++	355	+	395	++
236	++	276	+++	316	+	356	++	396	+++
237	+++	277	+++	217	+++	357	++	397	++
238	+++	278	+++	318	+++	358	++	398	+++
239	+	279	+	319	+++	259	++	399	+++
240	++	280	++	320	+++	360	+++	400	++

[Table 3-3]

Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity
401	+++	441	+++	481	+	521	+++	561	++
402	+++	442	++	482	+++	522	+++	562	+++
403	+++	443	++	483	+++	523	++	563	+
404	+++	444	+++	484	+++	524	++	564	++
405	+++	445	+++	485	+++	525	+++	565	+
406	+++	446	+++	486	+	526	+++	566	++
407	+++	447	+++	487	+	527	+++	567	++
408	++	448	+++	488	+	528	++	568	+
409	++	449	+	489	+	529	+++	569	+
410	++	450	+	490	+	530	+++	570	++
411	++	451	+	491	++	531	+++	571	+
412	++	452	+	492	++	532	+++	572	++
413	+++	453	+	493	+++	533	+	573	++
414	+	454	+++	494	++	534	++	574	++
415	+	455	+	495	++	535	+	575	+++
416	+	456	+	496	+++	536	+++	576	+++
417	+	457	+	497	+	537	+	577	++
418	++	458	+++	498	+++	538	++	578	++
419	+	459	+++	499	+++	539	++	579	++
420	++	460	+	500	+++	540	+	580	++
421	++	461	+++	501	+++	541	+++	581	+
422	++	462	+	502	+++	542	+++	582	+
423	++	463	+	503	+++	543	+++	583	+
424	+	464	+	504	+	544	+++	584	+
425	+	465	+	505	+++	545	++	585	+

(continued)

Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity
426	+++	466	+	506	+++	546	++	586	+
427	++	467	+++	507	+++	547	++	587	+++
428	++	468	+++	508	+++	548	+	588	++
429	+++	469	+++	509	+++	549	++	589	++
430	+++	470	+++	510	+++	550	+++	590	+
431	++	471	+++	511	+	551	++	591	+
432	+++	472	++	512	++	552	+	592	+++
433	++	473	++	513	++	553	+	593	+
434	+++	474	+	514	++	554	+	594	+
435	+	475	+	515	++	555	+	595	++
436	+	476	++	516	+	556	++	596	++
437	++	477	+++	517	+++	557	++	597	++
438	++	478	++	518	++	558	++	598	++
439	+++	479	+	519	++	559	++	599	+++
440	+++	480	+	520	++	560	++	600	++

[Table 3-4]

Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity
601	++	641	++	681	+	721	+	761	+
602	++	642	+++	682	++	722	++	762	+
603	++	643	++	683	+	723	++	763	+
604	+++	644	+++	684	+	724	+++	764	++
605	++	645	++	685	+	725	+	765	+++
606	++	646	++	686	+	726	++	766	+
607	+	647	+	687	+	727	++	767	+++
608	+	648	+	688	++	728	++	768	+++
609	+++	649	++	689	++	729	++	769	+++
610	+++	650	++	690	++	730	++	770	+++
611	+	651	+++	691	+++	731	+	771	++
612	+	652	+++	692	+	732	++	772	+++
613	++	653	++	693	++	733	+	773	+++
614	+	654	+	694	++	734	+++	774	+++
615	+	655	+++	695	+++	735	+++	775	+++
616	++	656	+++	696	+++	736	++	776	+
617	++	657	+++	697	+++	737	+++	777	+
618	++	658	++	698	++	738	++	778	+
619	+++	659	++	699	+	739	++	779	+
620	++	660	+	700	+	740	+	780	+
621	+++	661	+	701	+++	741	++	781	+
622	+++	662	++	702	+++	742	+++	782	+
623	+++	663	++	703	++	743	+++	783	+
624	+++	664	++	704	+++	744	++	784	+
625	+++	665	+	705	++	745	+	785	++

(continued)

Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity
626	+++	666	+	706	+++	746	+	786	+++
627	+++	667	++	707	++	747	+	787	+++
628	+++	668	+++	708	+++	748	+++	788	+
629	+++	669	++	709	++	749	++	789	++
630	++	670	+++	710	++	750	++	790	++
631	++	671	+++	711	+++	751	+	791	++
632	++	672	+++	712	++	752	++	792	++
633	++	673	+	713	++	753	+	793	+
634	+++	674	++	714	+++	754	+++	794	++
635	+	675	++	715	+++	755	++	795	+++
636	+	676	+	716	++	756	+	796	++
637	+++	677	+	717	++	757	+	797	+
638	++	678	+	718	+++	758	+++	798	++
639	+	679	+	719	++	759	+++	799	+++
640	++	680	+	720	+	760	+++	800	++

[Table 3-5]

Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity
801	+++	841	+	881	+	921	+	961	+
802	+++	842	+++	882	+	922	+	962	++
803	+++	843	+	883	++	923	++	963	+++
804	++	844	+	884	++	924	++	964	++
805	++	845	+	885	+	925	+	965	++
806	++	846	++	886	+	926	+	966	+++
807	++	847	+	887	++	927	++	967	++
808	+++	848	+++	888	++	928	++	968	+++
809	+++	849	+++	889	+	929	+	969	+++
810	+++	850	+++	890	++	930	++	970	+
811	+++	851	+	891	++	931	++	971	+
812	+++	852	+	892	++	932	+++	972	+++
813	+	853	++	893	+	933	+	973	++
814	+	854	+++	894	+	934	++	974	++
815	++	855	++	895	+	935	+++	975	+++
816	+	856	+++	896	++	936	++	976	++
817	+	857	+++	897	+	937	+++	977	+++
818	++	858	++	898	+	938	++	978	+++
819	++	859	+++	899	++	939	++	979	+++
820	+	860	+++	900	+++	940	+	980	+++
821	++	861	+++	901	+	941	+	981	++
822	+++	862	++	902	++	942	+	982	++
823	+++	863	+	903	+++	943	+	983	+++
824	++	864	++	904	+++	944	++	984	++
825	++	865	+	905	+++	945	+++	985	+++

(continued)

Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity
826	+++	866	+++	906	+++	946	++	986	++
827	+++	867	+	907	+++	947	+	987	+++
828	+++	868	++	908	+++	948	+++	988	+++
829	++	869	+	909	+++	949	+++	989	+++
830	++	870	++	910	+++	950	+++	990	+++
831	+	871	+	911	++	951	+++	991	+++
832	+++	872	+++	912	+++	952	+++	992	+++
833	+++	873	+++	913	+++	953	+++	993	++
834	+++	874	+++	914	+++	954	++	994	++
835	+++	875	+++	915	+++	955	+++	995	++
836	++	876	+++	916	+++	956	++	996	+++
837	++	877	+++	917	++	957	+++	997	++
838	++	878	+++	918	+	958	+++	998	++
839	+	879	+	919	++	959	++	999	++
840	+	880	++	920	+	960	++	1000	+++

[Table 3-6]

Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity
1001	+++	1041	++	1081	++	1121	+	1161	++
1002	+	1042	+++	1082	+	1122	+	1162	++
1003	++	1043	+++	1083	++	1123	+	1163	++
1004	++	1044	+++	1084	++	1124	+	1164	++
1005	+	1045	+++	1085	++	1125	+	1165	+
1006	++	1046	+++	1086	+++	1126	+	1166	+
1007	++	1047	+++	1087	+++	1127	+	1167	+++
1008	++	1048	+++	1088	++	1128	+	1168	++
1009	++	1049	+++	1089	++	1129	+++	1169	+
1010	+++	1050	++	1090	+	1130	+++	1170	+
1011	+++	1051	+++	1091	++	1131	+++	1171	++
1012	+++	1052	++	1092	++	1132	++	1172	++
1013	+++	1053	+	1093	+	1133	+	1173	+++
1014	+++	1054	+++	1094	++	1134	+	1174	++
1015	++	1055	+	1095	+	1135	+++	1175	+
1016	++	1056	++	1096	++	1136	+	1176	++
1017	+++	1057	+++	1097	+++	1137	+++	1177	+
1018	+++	1058	+++	1098	+	1138	++	1178	+
1019	++	1059	+++	1099	+	1139	++	1179	+
1020	++	1060	+++	1100	+	1140	++	1180	+
1021	++	1061	+++	1101	++	1141	++	1181	+
1022	+	1062	+++	1102	++	1142	++	1182	+
1023	++	1063	+++	1103	++	1143	+++	1183	+
1024	++	1064	++	1104	+	1144	+++	1184	+++
1025	+++	1065	+++	1105	++	1145	+++	1185	+++

(continued)

Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity
1026	+++	1066	+++	1106	+++	1146	++	1186	+++
1027	+++	1067	+	1107	+++	1147	+++	1187	+++
1028	+++	1068	++	1108	++	1148	+++	1188	++
1029	+++	1069	+	1109	++	1149	+++	1189	++
1030	+++	1070	+	1110	+++	1150	+++	1190	++
1031	+++	1071	+++	1111	++	1151	+++	1191	++
1032	+++	1072	+++	1112	+	1152	+++	1192	+
1033	+++	1073	+++	1113	+	1153	+++	1193	++
1034	++	1074	+++	1114	+	1154	+++	1194	+
1035	+++	1075	+++	1115	+	1155	+++	1195	+++
1036	+	1076	+++	1116	+	1156	+++	1196	++
1037	+++	1077	+++	1117	++	1157	++	1197	++
1038	++	1078	+++	1118	+	1158	+	1198	++
1039	++	1079	+++	1119	++	1159	++	1199	+++
1040	++	1080	+++	1120	+++	1160	+	1200	++

[Table 3-7]

Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity
1201	++	1242	++	1283	+	1324	+++	1365	+
1202	+++	1243	+++	1284	++	1325	+++	1366	+++
1203	+++	1244	+++	1285	+	1326	++	1367	+++
1204	++	1245	++	1286	+	1327	++	1368	+++
1205	+++	1246	++	1287	+	1328	++	1369	+++
1206	+++	1247	++	1288	+	1329	+	1370	++
1207	+++	1248	++	1289	+	1330	+++	1371	+++
1208	+++	1249	+++	1290	++	1331	+	1372	+
1209	++	1250	++	1291	+	1332	+	1373	+++
1210	+++	1251	++	1292	++	1333	++	1374	++
1211	+++	1252	++	1293	++	1334	+++	1375	++
1212	+++	1253	++	1294	+	1335	+++	1376	++
1213	++	1254	++	1295	+++	1336	++	1377	++
1214	+++	1255	+++	1296	+++	1337	+++	1378	++
1215	+++	1256	++	1297	++	1338	+++	1379	+
1216	++	1257	++	1298	++	1339	+++	1380	+++
1217	+++	1258	+++	1299	+++	1340	+++	1381	+
1218	+++	1259	+++	1300	+++	1341	++	1382	++
1219	+++	1260	++	1301	+++	1342	++	1383	++
1220	+	1261	+	1302	+++	1343	++	1384	++
1221	++	1262	+	1303	+	1344	+	1385	++
1222	++	1263	+	1304	+++	1345	++	1386	++
1223	+	1264	++	1305	++	1346	+++	1387	+++
1224	++	1265	++	1306	+++	1347	++	1388	++
1225	++	1266	++	1307	+	1348	+++	1389	++

(continued)

Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity	Compound number	Inhibitory activity
1226	++	1267	+	1308	++	1349	++	1390	++
1227	++	1268	++	1309	++	1350	+++	1391	++
1228	++	1269	+	1310	++	1351	+	1392	+
1229	++	1270	++	1311	++	1352	++	1393	++
1230	+	1271	+	1312	+++	1353	++	1394	++
1231	++	1272	++	1313	++	1354	+++	1395	+++
1232	+	1273	++	1314	++	1355	++	1396	++
1233	+++	1274	++	1315	++	1356	++	1397	++
1234	+++	1275	+	1316	+++	1357	+++	1398	+++
1235	++	1276	+	1317	+++	1358	++	1399	+
1236	++	1277	++	1318	++	1359	++	1400	++
1237	+++	1278	++	1319	++	1360	+++	1401	++
1238	+	1279	+++	1320	++	1361	+++	1402	++
1239	+++	1280	+++	1321	++	1362	++	1403	++
1240	+++	1281	++	1322	+++	1363	+	1404	+++
1241	+++	1282	++	1323	+++	1364	+	1405	+

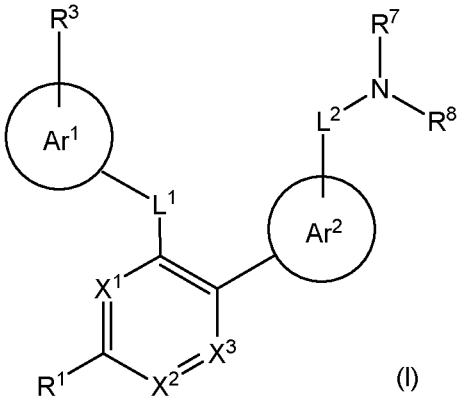
[Industrial applicability]

[0507] The compound of the present invention is used as a pharmaceutical product.

Claims

1. A compound represented by the formula (I) or a pharmaceutically acceptable salt thereof.

[Chem. 1]



(I)

[wherein,

X^1, X^2, and X^3 are independently CH, N, or CY;
At least one of X^1, X^2, and X^3 is CH or CY;
Y is a halogen atom, or a C_{1-3} alkyl group optionally substituted with 1 to 3 halogen atoms;
R^1 is a cyano group, a fluorine atom, or a chlorine atom;
L^1 is -O-, -S-, -SO-, -CH(R^{11})-, -C(= CH_2)-, -CO-, 1,1-cyclopropylidene group, or -NR^{12}-;
R^{11} is a hydrogen atom, a hydroxy group, a C_{1-3} alkyl group optionally substituted with 1 to 3 halogen atoms, or a C_{1-3} alkoxy group optionally substituted with 1 to 2 cyano groups;
R^{12} is a hydrogen atom, or a C_{1-3} alkyl group optionally substituted with 1 to 3 halogen atoms;
Ar^1 is a nitrogen-containing heteroaryl ring optionally substituted with 1 to 3 R^2;
R^2 is independently a halogen atom, a cyano group, or a C_{1-4} alkyl group optionally substituted with 1 to 3 halogen atoms;
R^3 is a hydrogen atom, a halogen atom, an amino group, a cyano group, a carboxy group, a (C_{1-3} alkylcarbonyl)amino group, a (C_{1-6} alkylamino)carbonyl group, a di(C_{1-3} alkyl)aminocarbonyl group, a (C_{1-3} alkoxy)carbonyl group, a (C_{3-8} cycloalkyl)amino group, a (C_{3-8} heterocycloalkyl)amino group, a C_{3-8} cycloalkyl group, a 3- to 8-membered heterocycloalkyloxy group, a C_{3-8} cycloalkyloxy group optionally substituted with 1 to 6 R^{31}, a C_{1-6} alkyl group optionally substituted with 1 to 6 R^{31}, a C_{1-6} alkoxy group optionally substituted with 1 to 6 R^{31}, a di(C_{1-6} alkyl)amino group optionally substituted with 1 to 6 R^{31}, a (C_{1-6} alkyl)amino group optionally substituted with 1 to 6 R^{31}, a 3- to 8-membered heterocycloalkyl group optionally substituted with 1 to 4 R^{32}, an aryl group optionally substituted with 1 to 4 R^{32}, or a heteroaryl group optionally substituted with 1 to 4 R^{32};
R^{31} is independently a halogen atom, a hydroxy group, a cyclopropylidene group, a C_{3-8} cycloalkyl group optionally substituted with 1 to 3 halogen atoms, a 3- to 8-membered heterocycloalkyl group, an oxetanylidene group, a C_{1-4} alkoxy group, or a 3- to 8-membered cycloalkyloxy group;
R^{32} is independently a halogen atom, a hydroxy group, an acetylamino group, a C_{1-3} alkyl group optionally substituted with 1 to 3 halogen atoms, a C_{1-3} alkoxy group optionally substituted with 1 to 3 halogen atoms, an oxo group, a cyano group, a carboxy group, a (C_{1-3} alkoxy)carbonyl group, a (C_{1-3} alkyl)sulfonyl group, a carboxamide group, or a benzyloxy group;
when R^2 and R^3 are bonded to atoms adjacent to each other on Ar^1, R^2 and R^3 may be bonded via a single bond or -O- to form a 5- to 7-membered ring together with the atoms of Ar^1 to which they are bonded;
Ar^2 is an aryl ring optionally substituted with 1 to 4 R^4, or a heteroaryl ring optionally substituted with 1 to 4 R^4;
R^4 is independently a halogen atom, a hydroxy group, a carboxy group, a cyano group, a cyanomethyl group,

an amino group, a di(C_{1-3} alkyl)amino group, a C_{1-3} alkyl group optionally substituted with 1 to 3 halogen atoms, or C_{1-3} alkoxy group;
L^2 is a single bond, a C_{1-6} alkylene group optionally substituted with 1 to 3 R^{21}, a C_{3-8} cycloalkylene group optionally substituted with 1 to 3 R^{21}, or a 4- to 8-membered heterocycloalkylene group optionally substituted with 1 to 3 R^{21},
L^2 may be bonded at any position to Ar^2 or $-NR^7R^8$ which is located at either end thereof;
One sp^3 carbon atom at any position of L^2 may be replaced by a structure of - O- or $-NR^{22}$-;
R^{21} is independently a halogen atom, a hydroxy group, an oxo group, a cyano group, a 1,1-cyclopropylidene group, an oxetanylidene group, a carboxy group, a carboxamide group, a C_{1-6} alkyl group optionally substituted with 1 to 3 halogen atoms, a C_{3-8} cycloalkyl group, a C_{1-6} alkoxy group, a (C_{1-3} alkoxy)C_{1-3} alkyl group, a (C_{1-3} alkoxy) C_{1-3} alkoxy group, a (hydroxy) C_{1-6} alkyl group, a (carboxy)C_{1-3} alkyl group, a (carboxy)C_{1-3} alkoxy group, a (C_{1-3} alkoxy)carbonyl group, a (C_{1-3} alkoxycarbonyl)C_{1-3} alkyl group, a (C_{1-6} alkylamino)carbonyl group, a di(C_{1-3} alkyl) aminocarbonyl group, a phenyl group optionally substituted with 1 to 3 halogen atoms, a heteroaryl group optionally substituted with 1 to 3 halogen atoms, or a phenoxy group optionally substituted with 1 to 3 halogen atoms;
R^{22} is a hydrogen atom or a C_{1-3} alkyl group;
L^2 and R^7 may be bonded via a single bond, -O-, $-S(=O)_n$-, or $-NR^{23}$-, to form a 4- to 8-membered ring containing a nitrogen atom to which L^2 and R^7 are bonded, and the ring is optionally substituted with 1 to 3 halogen atoms or 1 to 2 hydroxy groups;
n represents an integer from 0 to 2;
R^{23} is a hydrogen atom or a C_{1-3} alkyl group;
when L^2 and R^4 are bonded to atoms adjacent to each other on Ar^2, they may be bonded via a single-bond or -O- to form a 5- to 8-membered ring together with the atoms of Ar^2 to which they are bonded;
R^7 is a hydrogen atom, or C_{1-3} alkyl group;
R^7 and an atom of Ar^2 may be bonded via a single bond to form a 5- to 8-membered ring;
R^8 is a hydrogen atom, a C_{1-6} alkyl group, an adamantyl group, a C_{1-6} cycloalkyl group, a cyanomethyl group, an oxetanyl group, a (C_{1-3} alkylamino)carbonylmethyl group, a di(C_{1-3} alkyl)aminocarbonylmethyl group, a (C_{1-3} alkylamino)C_{1-8} alkyl group, a di(C_{1-3} alkyl)aminoC_{1-8} alkyl group, a (hydroxy)C_{1-8} alkyl group, a (carboxy)C_{1-3} alkyl group, a (C_{1-3} alkoxycarbonyl)C_{1-3} alkyl group, or a (C_{1-3} alkoxy)C_{1-3} alkyl group;
R^7 and R^8 may be bonded each other via a single bond, -O-, $-S(=O)_m$-, or $-NR^{41}$-to form a 3- to 8-membered ring, and further, the ring is optionally substituted with an amino group, an oxo group, or a C_{1-3} alkyl group;
m represents an integer from 0 to 2;
R^{41} is a hydrogen atom or a C_{1-3} alkyl group.]

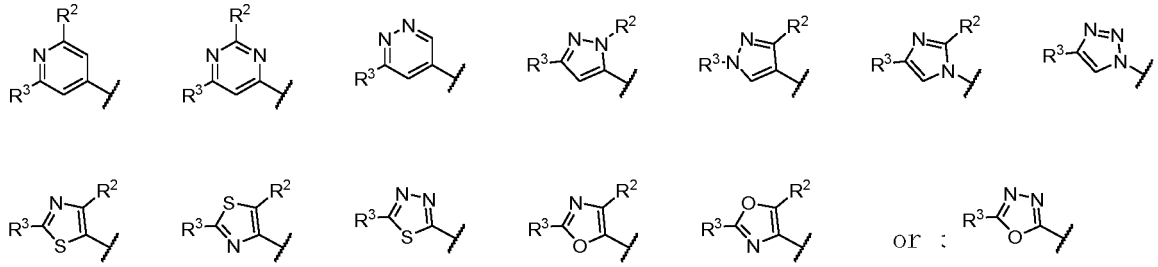
2. The compound according to claim 1 or a pharmaceutically acceptable salt thereof, wherein X^1, X^2, and X^3 are CH.

3. The compound according to claim 1 or claim 2 or a pharmaceutically acceptable salt thereof, wherein R^1 is a cyano group.

4. The compound according to claim 1 or claim 2 or a pharmaceutically acceptable salt thereof, wherein R^1 is a fluorine atom.

5. The compound according to any one of claims 1 to 4 or a pharmaceutically acceptable salt thereof, wherein the nitrogen-containing heteroaryl ring of Ar^1 is one of the following groups:

[Chem. 2]



6. The compound according to any one of claims 1 to 5 or a pharmaceutically acceptable salt thereof, wherein L^1 is -O-.

7. The compound according to any one of claims 1 to 5 or a pharmaceutically acceptable salt thereof, wherein L^1 is -CO-.

8. The compound according to any one of claims 1 to 5 or a pharmaceutically acceptable salt thereof, wherein L^1 is $-CH_2-$.

9. The compound according to any one of claims 1 to 8 or a pharmaceutically acceptable salt thereof, wherein R^2 is a methyl group.

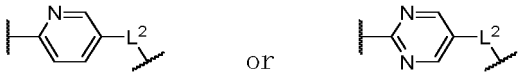
10. The compound according to any one of claims 1 to 9 or a pharmaceutically acceptable salt thereof, wherein R^3 is a C_{3-8} cycloalkyl group, a 3- to 8-membered heterocycloalkyloxy group, a C_{3-8} cycloalkyloxy group optionally substituted with 1 to 6 R^{31}, a C_{1-6} alkyl group optionally substituted with 1 to 6 R^{31}, a C_{1-6} alkoxy group optionally substituted with 1 to 6 R^{31}, a di(C_{1-6} alkyl)amino group optionally substituted with 1 to 6 R^{31}, a (C_{1-6} alkyl)amino group optionally substituted with 1 to 6 R^{31}, a 3- to 8-membered heterocycloalkyl group optionally substituted with 1 to 4 R^{32}, an aryl group optionally substituted with 1 to 4 R^{32}, or a heteroaryl group optionally substituted with 1 to 4 R^{32}.

11. The compound according to any one of claims 1 to 10 or a pharmaceutically acceptable salt thereof, wherein R^{31} is a halogen atom, a cyclopropylidene group, or a C_{1-4} alkoxy group.

12. The compound according to any one of claims 1 to 11 or a pharmaceutically acceptable salt thereof, wherein R^{32} is a halogen atom, a C_{1-3} alkyl group optionally substituted with 1 to 3 halogen atoms, a C_{1-3} alkoxy group optionally substituted with 1 to 3 halogen atoms, an oxo group or a cyano group.

13. The compound according to any one of claims 1 to 12 or a pharmaceutically acceptable salt thereof, wherein the heteroaryl ring of Ar^2 is

[Chem. 3]



14. The compound according to any one of claims 1 to 13 or a pharmaceutically acceptable salt thereof, wherein L^2 is a C_{1-3} alkylene group optionally substituted with 1 to 2 R^{21}.

15. The compound according to any one of claims 1 to 13 or a pharmaceutically acceptable salt thereof, wherein L^2 is $-CH_2-$.

16. The compound according to any one of claims 1 to 13 or a pharmaceutically acceptable salt thereof, wherein L^2 is $-CH_2CH_2-$.

17. The compound according to any one of claims 1 to 16 or a pharmaceutically acceptable salt thereof, wherein R^7 is a hydrogen atom.

18. The compound according to any one of claims 1 to 17 or a pharmaceutically acceptable salt thereof, wherein R^8 is a hydrogen atom.

19. The compound according to claim 1 or a pharmaceutically acceptable salt thereof, wherein the compound represented by the formula (I) is selected from the following (1) to (150):

(1) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
(2) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
(3) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
(4) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-methyl-5-(5-methylpyridin-2-yl)pyrazol-3-yl]oxybenzonitrile
(5) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-[5-(4-fluorophenyl)-2-methylpyrazol-3-yl]oxybenzonitrile
(6) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-[5-(3-fluorophenyl)-2-methylpyrazol-3-yl]oxybenzonitrile
(7) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
(8) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-methyl-5-(2-methylpropyl)pyrazol-3-yl]oxybenzonitrile

(9) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxybenzonitrile
(10) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-5-propylpyrazol-3-yl)oxybenzonitrile
(11) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(5-cyclobutyl-2-methylpyrazol-3-yl)oxybenzonitrile
(12) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3 -(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
(13) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-6-pyrrolidin-1-ylpyridin-4-yl)oxybenzonitrile
(14) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-6-pyridin-2-ylpyridin-4-yl)oxybenzonitrile
(15) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-propylpyrazol-3-yl)oxybenzonitrile
(16) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxybenzonitrile
(17) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-pyrrolidin-1-ylpyridin-4-yl)oxybenzonitrile
(18) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-methyl-5-(trifluoromethyl)pyrazol-3-yl]oxybenzonitrile
(19) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-cyclobutyl-2-methylpyrazol-3-yl)oxybenzonitrile
(20) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
(21) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-phenylpyrimidin-4-yl)oxybenzonitrile
(22) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(6-phenylpyridazin-4-yl)oxybenzonitrile
(23) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
(24) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(5-ethyl-2-methylpyrazol-3-yl)oxybenzonitrile
(25) 4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
(26) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-ethyl-2-methylpyrazol-3-yl)oxybenzonitrile
(27) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[6-(2-cyanophenyl)-2-methylpyrimidin-4-yl]oxybenzonitrile
(28) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2,5-dimethylpyrazol-3-yl)oxybenzonitrile
(29) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-phenylpyrazol-3-yl)oxybenzonitrile
(30) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
(31) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-butyl-2-methylpyrazol-3-yl)oxybenzonitrile
(32) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-(5-ethyl-2-methylpyrazol-3-yl)oxybenzonitrile
(33) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
(34) 4-[5-(aminomethyl)pyridin-2-yl]-3-(5-ethyl-2-methylpyrazol-3-yl)oxybenzonitrile
(35) 4-[5-(aminomethyl)pyridin-2-yl]-3-(5-cyclopropyl-2-methylpyrazol-3-yl)oxybenzonitrile
(36) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
(37) 4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-6-morpholin-4-ylpyridin-4-yl)oxybenzonitrile
(38) 4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-5-propylpyrazol-3-yl)oxybenzonitrile
(39) 4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxybenzonitrile
(40) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-propylpyrazol-3-yl)oxybenzonitrile
(41) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxybenzonitrile
(42) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-tert-butyl-2-methylpyrazol-3-yl)oxybenzonitrile
(43) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-pyridin-2-ylpyridin-4-yl)oxybenzonitrile
(44) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-methyl-5-(1,3-thiazol-2-yl)pyrazol-3-yl]oxybenzonitrile
(45) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-(1,3-thiazol-2-yl)pyrazol-3-yl]oxybenzonitrile
(46) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-cyclopentyl-2-methylpyrazol-3-yl)oxybenzonitrile
(47) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
(48) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-(3-fluorophenyl)-2-methylpyrazol-3-yl]oxybenzonitrile
(49) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-[(2S)-2-(difluoromethyl)morpholin-4-yl]-6-methylpyridin-4-yl]oxybenzonitrile
(50) 4-[5-(aminomethyl)pyridin-2-yl]-3-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl]oxybenzonitrile
(51) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-[(2R)-2-(difluoromethyl)morpholin-4-yl]-6-methylpyridin-4-yl]oxybenzonitrile
(52) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)pyridin-4-yl]oxybenzonitrile
(53) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-piperidin-1-ylpyrimidin-4-yl)oxybenzonitrile
(54) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-pyrrolidin-1-ylpyrimidin-4-yl)oxybenzonitrile
(55) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)pyridin-4-yl]oxybenzonitrile
(56) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-[2-[2-methoxyethyl(methyl)amino]-6-methylpyridin-4-yl]oxybenzonitrile
(57) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(propan-2-ylamino)pyridin-4-yl]oxybenzonitrile
(58) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-[(3R)-3-methylmorpholin-4-yl]pyridin-4-yl]oxybenzonitrile
(59) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-[(3S)-3-methylmorpholin-4-yl]pyridin-4-yl]oxybenzonitrile
(60) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-5-piperidin-1-ylpyrazol-3-yl)oxybenzonitrile
(61) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-(2-methyl-5-pyrrolidin-1-ylpyrazol-3-yl)oxybenzonitrile
(62) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-[5-(dimethylamino)-2-methylpyrazol-3-yl]oxybenzonitrile

(63) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(1,3-thiazol-2-yl)pyrazol-3-yl]oxybenzonitrile
(64) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-6-pyridin-2-ylpyrimidin-4-yl)oxybenzonitrile
(65) 4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxybenzonitrile
(66) 4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-5-piperidin-1-ylpyrazol-3-yl)oxybenzonitrile
(67) 4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-5-pyrrolidin-1-ylpyrazol-3-yl)oxybenzonitrile
(68) 4-[5-(aminomethyl)pyridin-2-yl]-3-[5-(dimethylamino)-2-methylpyrazol-3-yl]oxybenzonitrile
(69) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(4-methylpyridin-2-yl)pyrazol-3-yl]oxybenzonitrile
(70) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-(diethylamino)-2-methylpyrazol-3-yl]oxybenzonitrile
(71) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-(diethylamino)-2-methylpyrazol-3-yl]oxybenzonitrile
(72) 4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-6-pyrrolidin-1-ylpyrimidin-4-yl)oxybenzonitrile
(73) 4-[5-(aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-pyrrolidin-1-ylpyrimidin-4-yl]oxybenzonitrile
(74) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[6-(7-azabicyclo[2.2.1]heptan-7-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile
(75) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[6-(7-azabicyclo[2.2.1]heptan-7-yl)-2-methylpyrimidin-4-yl]oxybenzonitrile
(76) 4-[5-(aminomethyl)pyridin-2-yl]-3-(6-piperidin-1-ylpyridazin-4-yl)oxybenzonitrile
(77) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[(5-phenyl-1,3,4-thiadiazol-2-yl)oxy]benzonitrile
(78) 4-[5-(2-aminoethyl)pyridin-2-yl]-3-[5-(diethylamino)-2-methylpyrazol-3-yl]oxybenzonitrile
(79) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-[methyl(2-methylpropyl)amino]pyrazol-3-yl]oxybenzonitrile
(80) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-[cyclopropylmethyl(methyl)amino]-2-methylpyrazol-3-yl]oxybenzonitrile
(81) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-[methyl(propyl)amino]pyrazol-3-yl]oxybenzonitrile
(82) 4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-5-morpholin-4-ylpyrazol-3-yl)oxybenzonitrile
(83) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-[methyl(propan-2-yl)amino]pyrazol-3-yl]oxybenzonitrile
(84) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-[2,2-difluoroethyl(methyl)amino]-2-methylpyrazol-3-yl]oxybenzonitrile
(85) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-[methyl(2,2,2-trifluoroethyl)amino]pyrazol-3-yl]oxybenzonitrile
(86) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-6-[(2S)-2-methylpyrrolidin-1-yl]pyrimidin-4-yl]oxybenzonitrile
(87) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[3-methyl-1-(2-methylpropyl)pyrazol-4-yl]oxybenzonitrile
(88) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[3-methyl-1-(2-methylpropyl)pyrazol-4-yl]oxybenzonitrile
(89) 4-[5-(aminomethyl)pyridin-2-yl]-3-[2-methyl-5-(trifluoromethyl)pyrazol-3-yl]oxybenzonitrile
(90) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(trifluoromethyl)pyrazol-3-yl]oxybenzonitrile
(91) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-(trifluoromethyl)pyrazol-3-yl]oxybenzonitrile
(92) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-(7-azabicyclo[2.2.1]heptan-7-yl)-6-methylpyridin-4-yl]oxybenzonitrile
(93) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-(7-azabicyclo[2.2.1]heptan-7-yl)-6-methylpyridin-4-yl]oxybenzonitrile
(94) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(3-methyl-1-pyridin-2-ylpyrazol-4-yl)oxybenzonitrile
(95) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-(3-methyl-1-pyridin-2-ylpyrazol-4-yl)oxybenzonitrile
(96) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[3-methyl-1-(2,2,2-trifluoroethyl)pyrazol-4-yl]oxybenzonitrile
(97) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-[ethyl(propan-2-yl)amino]-2-methylpyrazol-3-yl]oxybenzonitrile
(98) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-(2-methylpropoxy)pyrimidin-4-yl]oxybenzonitrile
(99) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[6-(diethylamino)-2-methylpyrimidin-4-yl]oxybenzonitrile
(100) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-[methyl(propan-2-yl)amino]pyrimidin-4-yl]oxybenzonitrile
(101) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-[(2R)-2-methylpyrrolidin-1-yl]pyrimidin-4-yl]oxybenzonitrile
(102) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-6-[(2S)-2-methylpyrrolidin-1-yl]pyrimidin-4-yl]oxybenzonitrile
(103) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(3,3,4,5-tetrafluoropyrrolidin-1-yl)pyrazol-3-yl]oxybenzonitrile
(104) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-[2,2-difluoroethyl(ethyl)amino]-2-methylpyrazol-3-yl]oxybenzonitrile
(105) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-[2,2-difluoroethyl(ethyl)amino]-2-methylpyrazol-3-yl]oxybenzonitrile

(106) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[2-methyl-5-(3,3,4,4-tetrafluoropyrrolidin-1-yl)pyrazol-3-yl]oxybenzonitrile
(107) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[1-(2-methylpropyl)pyrazol-4-yl]oxybenzonitrile
(108) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(1-pyridin-2-ylpyrazol-4-yl)oxybenzonitrile
(109) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[1-(2,2-dimethylpropyl)-3-methylpyrazol-4-yl]oxybenzonitrile
(110) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(1,3-thiazol-4-yl)pyrazol-3-yl]oxybenzonitrile
(111) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[3-ethyl-1-(2-methylpropyl)pyrazol-4-yl]oxybenzonitrile
(112) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[1-(2-methylpropyl)-3-(trifluoromethyl)pyrazol-4-yl]oxybenzonitrile
(113) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(4-methyl-1,3-thiazol-5-yl)pyrazol-3-yl]oxybenzonitrile
(114) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[2-methyl-5-(5-methyl-1,3-thiazol-4-yl)pyrazol-3-yl]oxybenzonitrile
(115) 2-[2-[4-fluoro-2-[3-methyl-1-(2-methylpropyl)pyrazol-4-yl]oxyphenyl]pyrimidin-5-yl]ethanamine
(116) 5-[2-[5-(2-aminoethyl)pyrimidin-2-yl]-5-fluorophenoxy]-N,N-diethyl-1-methylpyrazole-3-amine
(117) 2-[6-[4-fluoro-2-(2-methyl-5-morpholin-4-ylpyrazol-3-yl)oxyphenyl]pyridin-3-yl]ethanamine
(118) 2-[2-[4-fluoro-2-(2-methyl-5-pyridin-2-ylpyrazol-3-yl)oxyphenyl]pyrimidin-5-yl]ethanamine
(119) 2-[2-[4-fluoro-2-(2-methyl-5-pyrrolidin-1-ylpyrazol-3-yl)oxyphenyl]pyrimidin-5-yl]ethanamine
(120) 2-[6-[4-fluoro-2-(2-methyl-5-pyrrolidin-1-ylpyrazol-3-yl)oxyphenyl]pyridin-3-yl]ethanamine
(121) 5-[2-[5-(2-aminoethyl)pyrimidin-2-yl]-5-fluorophenoxy]-N-(2,2-difluoroethyl)-N,1-dimethylpyrazole-3-amine
(122) 5-[2-[5-(2-aminoethyl)pyridin-2-yl]-5-fluorophenoxy]-N-(2,2-difluoroethyl)-N,1-dimethylpyrazole-3-amine
(123) 5-[2-[5-(2-aminoethyl)pyrimidin-2-yl]-5-fluorophenoxy]-N-(2,2-difluoroethyl)-N-ethyl-1-methylpyrazole-3-amine
(124) 5-[2-[5-(2-aminoethyl)pyridin-2-yl]-5-fluorophenoxy]-N-(2,2-difluoroethyl)-N-ethyl-1-methylpyrazole-3-amine
(125) 5-[2-[5-(2-aminoethyl)pyridin-2-yl]-5-fluorophenoxy]-N,N-diethyl-1-methylpyrazole-3 -amine
(126) 5-[2-[5-(2-aminoethyl)pyridin-2-yl]-5-fluorophenoxy]-N,N,1-trimethylpyrazole-3-amine
(127) 2-[6-[4-fluoro-2-[2-methyl-5-(oxan-4-yl)pyrazol-3-yl]oxyphenyl]pyridin-3-yl]ethanamine
(128) [2-[4-fluoro-2-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxyphenyl]pyrimidin-5-yl]methanamine
(129) 2-[2-[4-fluoro-2-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxyphenyl]pyrimidin-5-yl]ethanamine
(130) 2-[6-[4-fluoro-2-(2-methyl-5-propan-2-ylpyrazol-3-yl)oxyphenyl]pyridin-3-yl]ethanamine
(131) 2-[6-[2-(5-cyclopropyl-2-methylpyrazol-3-yl)oxy-4-fluorophenyl]pyridin-3-yl]ethanamine
(132) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-ethyl-2-methylpyrazole-3-carbonyl)benzonitrile
(133) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-(5-ethyl-2-methylpyrazole-3-carbonyl)benzonitrile
(134) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-morpholin-4-ylpyrazole-3-carbonyl)benzonitrile
(135) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-morpholin-4-ylpyrazole-3-carbonyl)benzonitrile
(136) 4-[5-(aminomethyl)pyridin-2-yl]-3-(2-methyl-5-morpholin-4-ylpyrazole-3-carbonyl)benzonitrile
(137) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-(5-tert-butyl-2-methylpyrazole-3-carbonyl)benzonitrile
(138) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(5-tert-butyl-2-methylpyrazole-3-carbonyl)benzonitrile
(139) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-(diethylamino)-2-methylpyrazole-3-carbonyl]benzonitrile
(140) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(1-pyridin-2-ylpyrazole-4-carbonyl)benzonitrile
(141) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3 -(2-methyl-6-morpholin-4-ylpyridine-4-carbonyl)benzonitrile
(142) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-(dimethylamino)-2-methylpyrazole-3-carbonyl]benzonitrile
(143) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-(dimethylamino)-2-methylpyrazole-3-carbonyl]benzonitrile
(144) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-(diethylamino)-2-methylpyrazole-3-carbonyl]benzonitrile
(145) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-piperidin-1-ylpyrazole-3-carbonyl)benzonitrile
(146) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-piperidin-1-ylpyrazole-3-carbonyl)benzonitrile
(147) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-(2-methyl-5-pyrrolidin-1-ylpyrazole-3-carbonyl)benzonitrile
(148) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-(2-methyl-5-pyrrolidin-1-ylpyrazole-3-carbonyl)benzonitrile
(149) 4-[5-(2-aminoethyl)pyrimidin-2-yl]-3-[5-[2,2-difluoroethyl(ethyl)amino]-2-methylpyrazole-3-carbonyl]benzonitrile
(150) 4-[5-(aminomethyl)pyrimidin-2-yl]-3-[5-[2,2-difluoroethyl(ethyl)amino]-2-methylpyrazole-3-carbonyl]benzonitrile.

20. A pharmaceutical composition comprising the compound according to any one of claims 1 to 19 or a pharmaceutically acceptable salt thereof.

21. A pharmaceutical composition having TRPC6 channel inhibitory activity, comprising the compound according to any one of claims 1 to 19 or a pharmaceutically acceptable salt thereof.

22. A therapeutic or prophylactic agent for nephrotic syndrome, membranous nephropathy, acute renal failure, sepsis, chronic renal failure, diabetic nephropathy, pulmonary hypertension, acute lung injury, heart failure, malignant tumor, or muscular dystrophy, comprising the compound according to any one of claims 1 to 19 or a pharmaceutically acceptable salt thereof.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2021/015607

A. CLASSIFICATION OF SUBJECT MATTER
see extra sheet

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
Int. Cl. C07D213/74: A61K31/427, A61K31/4439, A61K31/444: A61K31/501: A61K31/506, A61K31/5377, A61K31/551: A61P3/10: A61P7/10: A61P9/04: A61P9/12: A61P11/00, A61P13/12: A61P21/04: A61P31/04: A61P35/00: A61P43/00: C07D237/20: C07D239/34: C07D239/42: C07D239/47, C07D239/48: C07D239/52, C07D401/10: C07D401/12: C07D401/14: C07D403/10: C07D403/12: C07D403/14: C07D417/04: C07D417/10, C07D417/12:

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Published examined utility model applications of Japan	1922-1996
Published unexamined utility model applications of Japan	1971-2021
Registered utility model specifications of Japan	1996-2021
Published registered utility model applications of Japan	1994-2021

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
CAplus/REGISTRY (STN)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2013/045519 A1 (GENFIT) 04 April 2013, pp. 21, 33	1-2, 4, 6, 14-15, 20
Y	US 4315926 A (CIBA-GEIGY CORPORATION) 16 February 1982, claims, example 4	1-2, 7, 15-16, 20
Y	ZHANG, L. et al. Experimental and Theoretical Studies on Ru(II)-Catalyzed Oxidative C-H/C-H Coupling of Phenols with Aromatic Amides Using Air as Oxidant: Scope, Synthetic Applications, and Mechanistic Insights, ACS Catalysis, 2018, vol. 8, no. 9, pp. 8324-8335, DOI 10.1021/acscatal.8b02816 scheme 4	1-2, 6, 14, 17

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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Date of the actual completion of the international search	Date of mailing of the international search report
18.05.2021	01.06.2021

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2021/015607

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International application No.
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